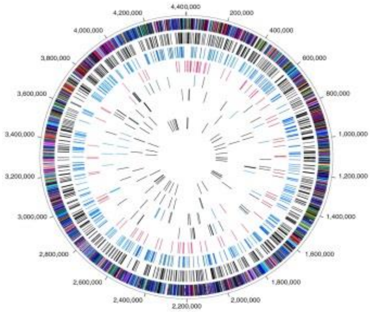
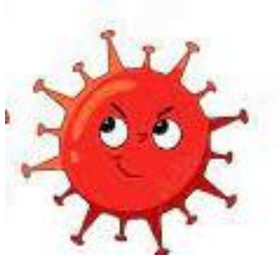
Infection Control Strategies:
Innovative strategies for infection control in hospitals.





Darío García de Viedma

Hospital General Universitario Gregorio Marañón, Madrid, Spain

IiSGM

ciberes
Centro de Investigación Biomédica en Red
Enfermedades Respiratorias

Human - Centric Indoor Climate for Healthcare Facilities (HumanIC)
HORIZON-MSCA-2022-DN-01

HumanIC

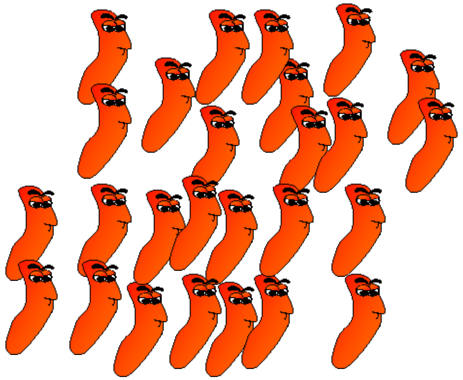
Warsaw February 27th 2024

Infection Control Strategies: Innovative strategies for infection control in hospitals.

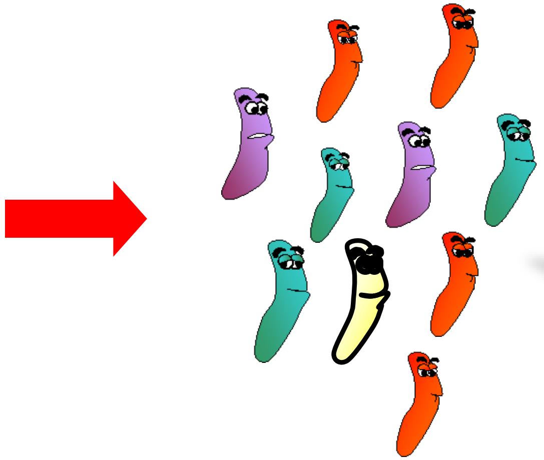
or

How to Use Genomic Epidemiology to understand transmission dynamics and orientate interventions

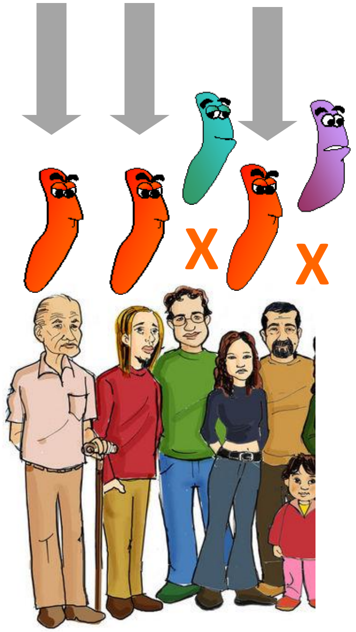
Genomic epidemiology



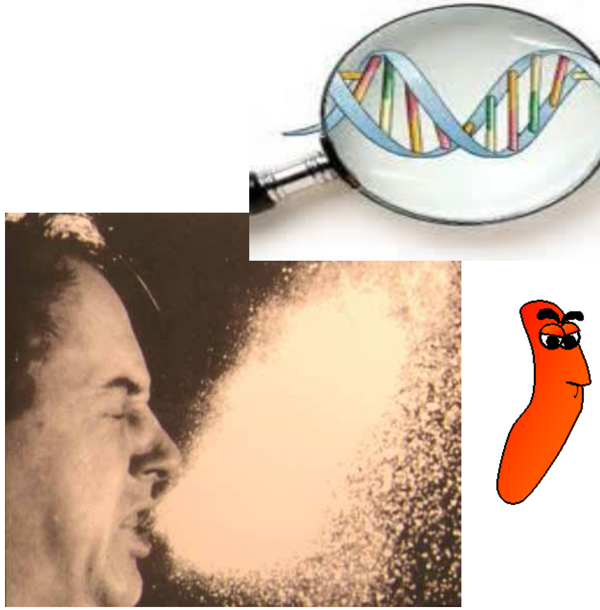
Bacteria X (Pseudomonas aeruginosa)



Different STRAINS

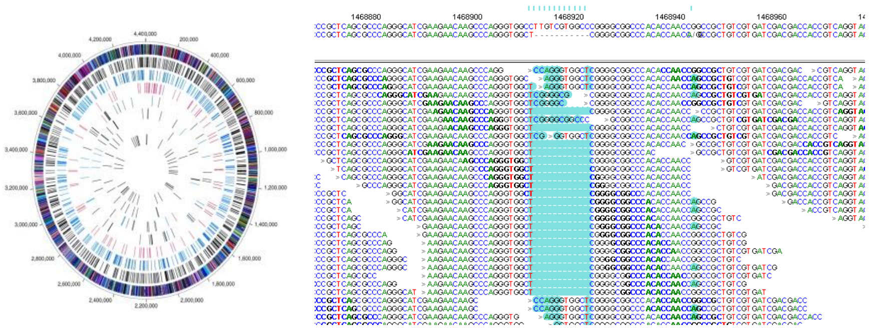


Orphan cases



Transmission CLUSTER

Genomic Epidemiology

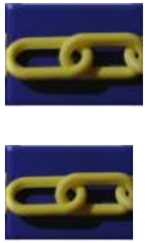


Quantitative analysis

Number of SNPs between bacteria from different patients

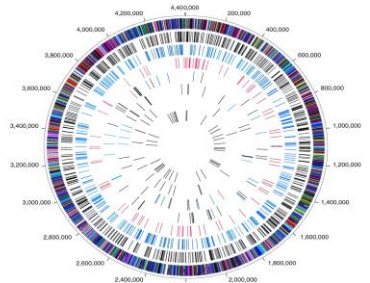
Number of SNPs

Transmission CLUSTER



Orphan cases

Genomic epidemiology in TB



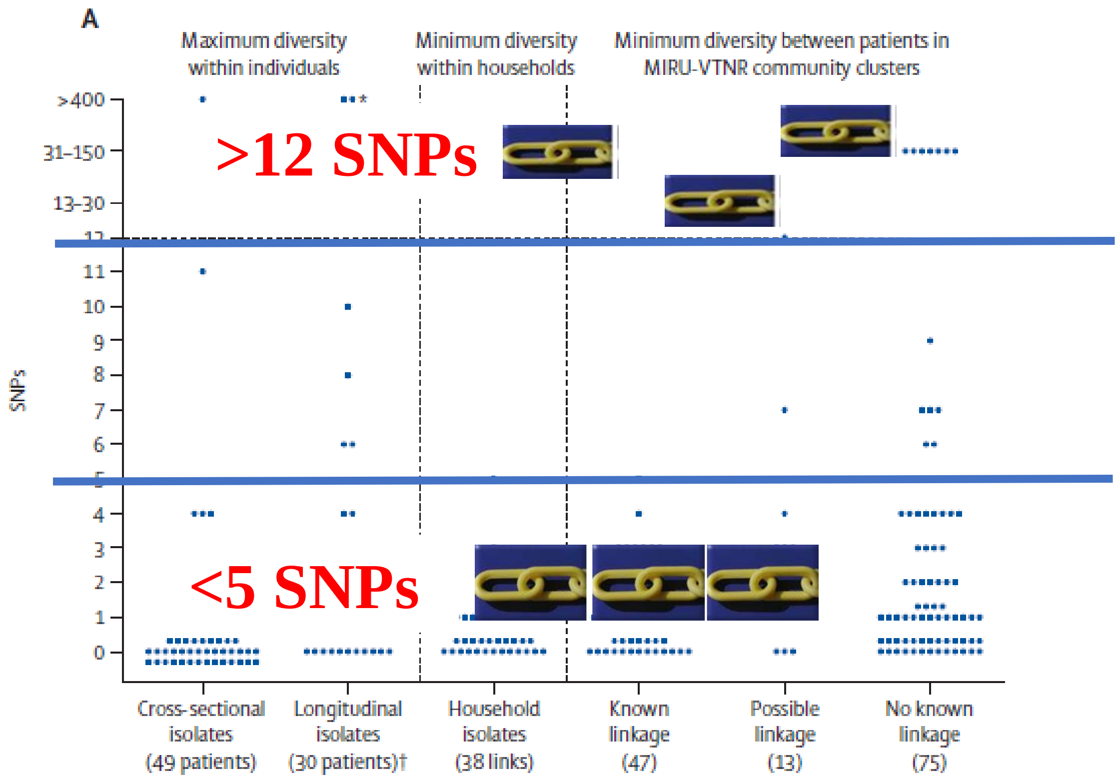
Whole Genome Sequencing

SNPs similarity thresholds to define clusters

Lancet ID, Nov 2012

Whole-genome sequencing to delineate *Mycobacterium tuberculosis* outbreaks: a retrospective observational study

Timothy M Walker*, Camilla L C Ip*, Ruth H Harrell*, Jason T Evans, Georgia Kapatai, Martin J Dedicoat, David W Eyre, Daniel J Wilson, Peter M Hawkey, Derrick W Crook, Julian Parkhill, David Harris, A Sarah Walker, Rory Bowden, Philip Monk†, E Grace Smith†, Tim E A Peto†

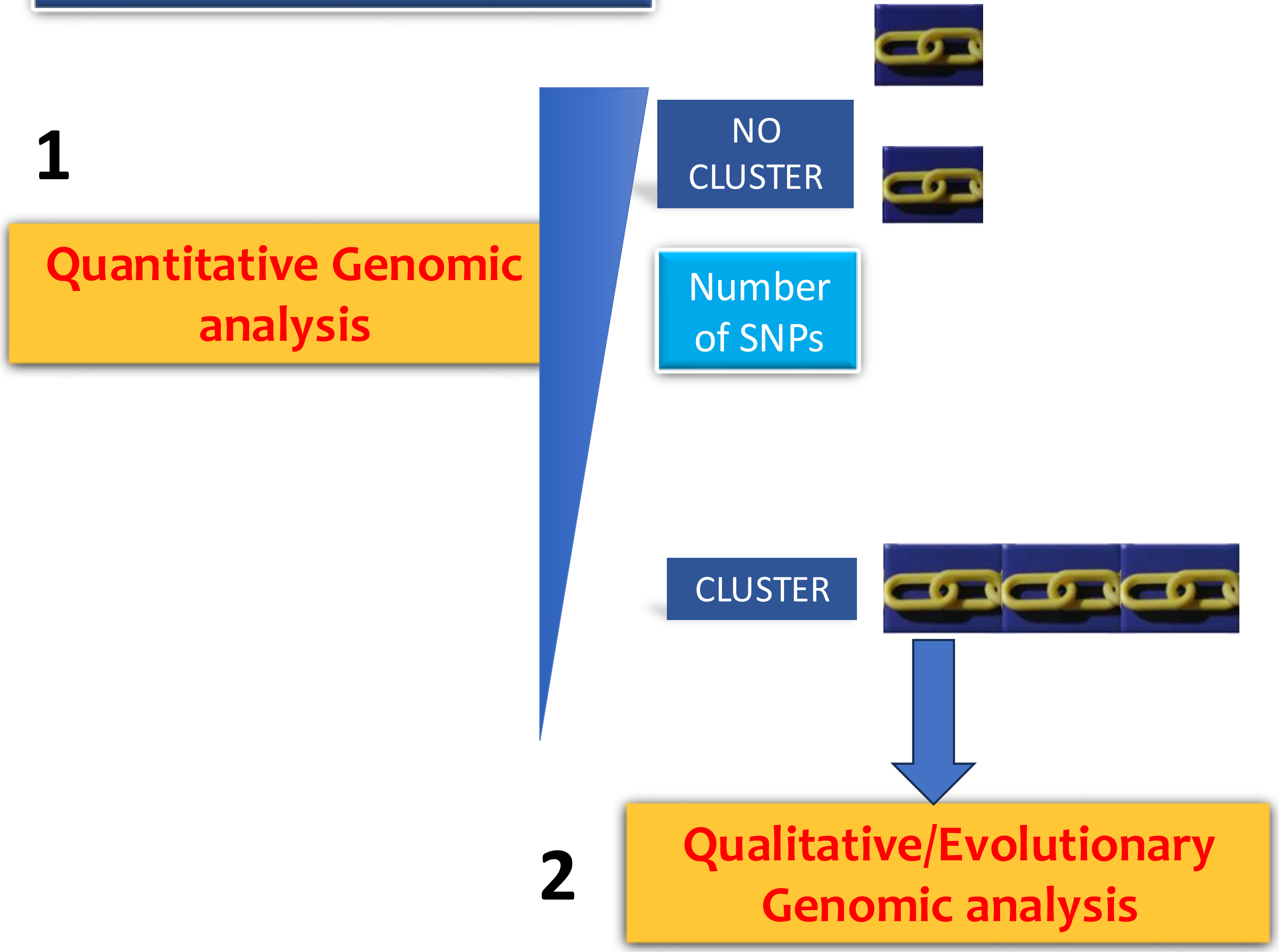


Different SNP thresholds for different bacteria

Genomic Epidemiology

HOSPITAL OUTBREAK **ALERT**

Higher number of cases
than expected



1

Quantitative Genomic analysis

NO CLUSTER

Number of SNPs

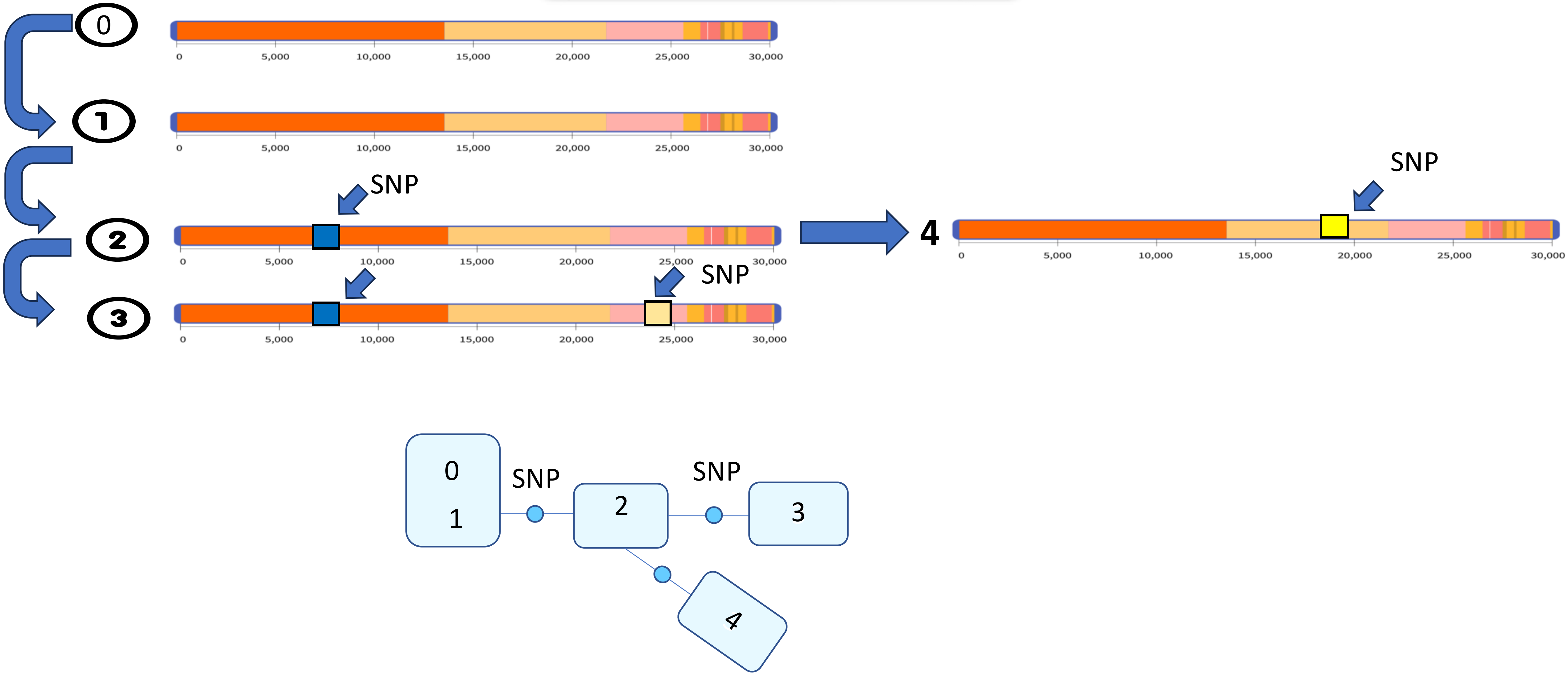
CLUSTER

2

Qualitative/Evolutionary Genomic analysis

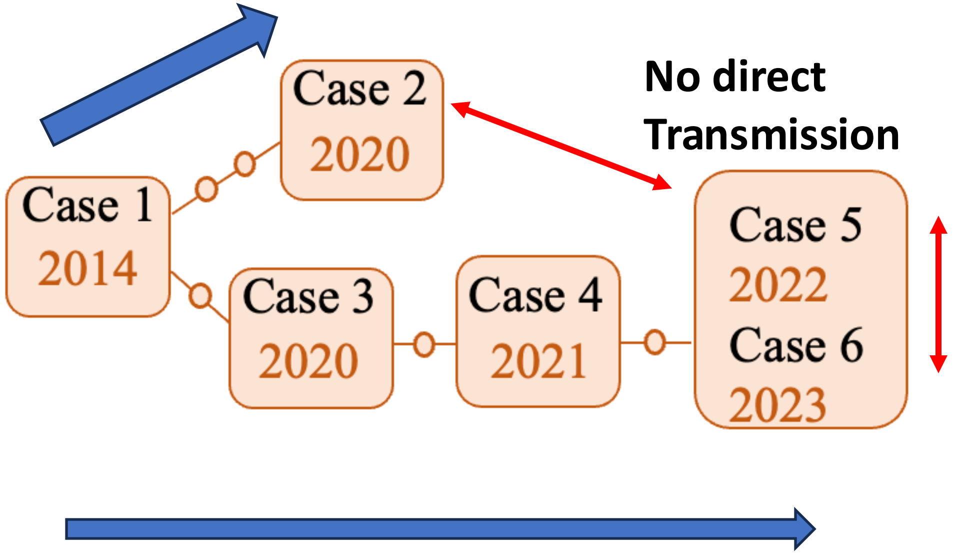
Qualitative evolutionary analysis

CLUSTER



Evolutionary analysis

Analysis of the **distribution** of SNPs



No direct Transmission

Direct Case-Case Transmission

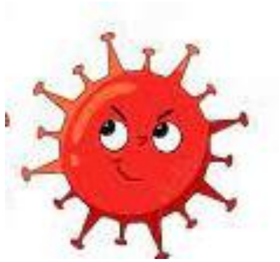
Genomic epidemiology

1. *Mycobacterium tuberculosis*

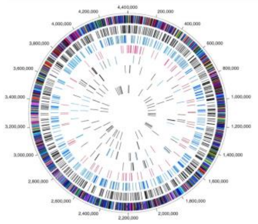
Genomic epidemiology

1. *Mycobacterium tuberculosis*

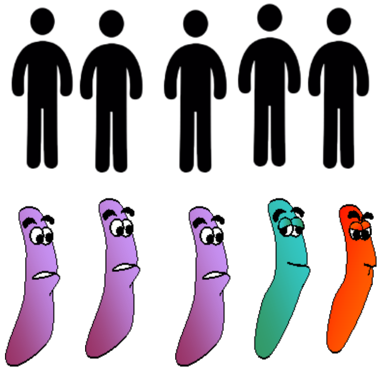
2. SARS-CoV-2



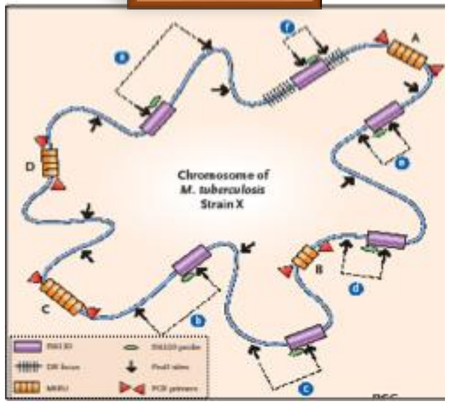
Genomic epidemiology



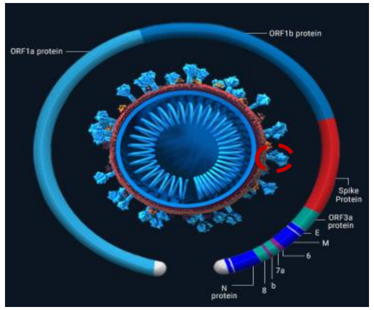
Mycobacterium tuberculosis



4.4 Mb



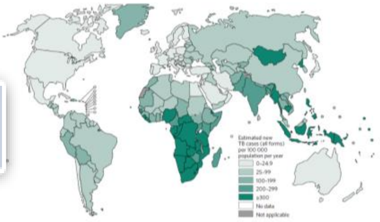
SARS-CoV-2



30Kb

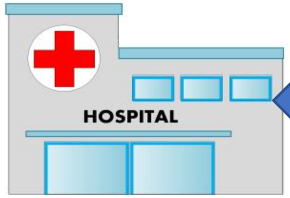
Populational

Global

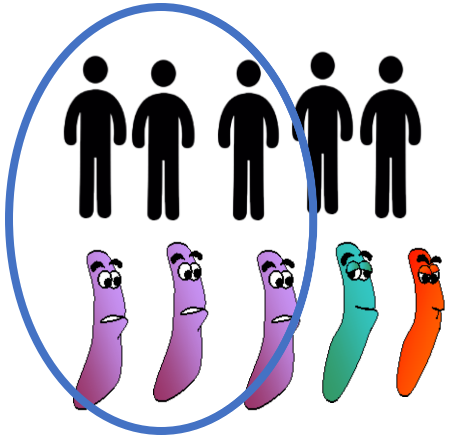


Local

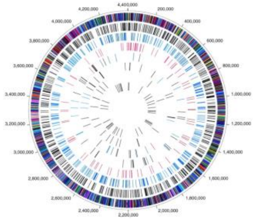
Hospital



Hospital (Nosocomial) transmission

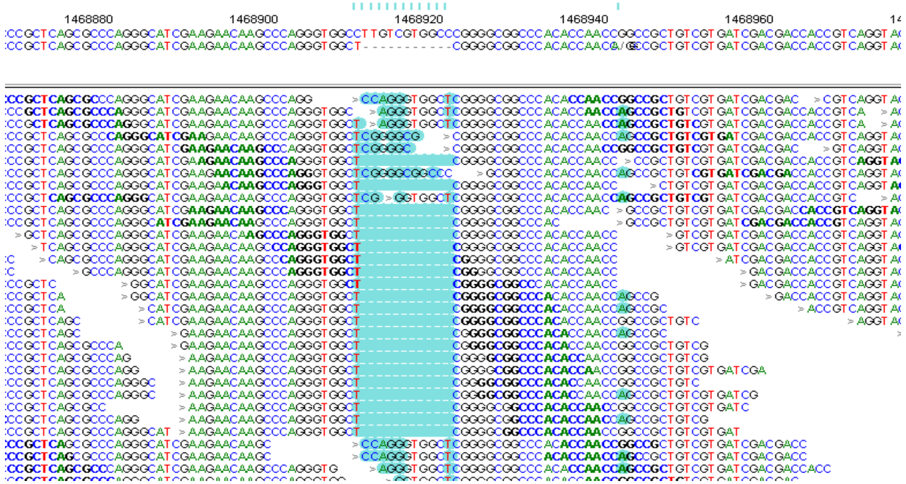


Genomic epidemiology



Mycobacterium tuberculosis

Epidemiological data



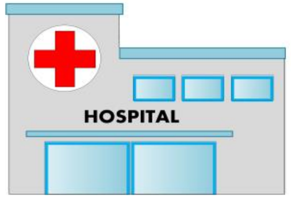
Understanding transmission dynamics

Transmission Hots spots

Tailor specific Control Measures

Replicate the model

Hospital

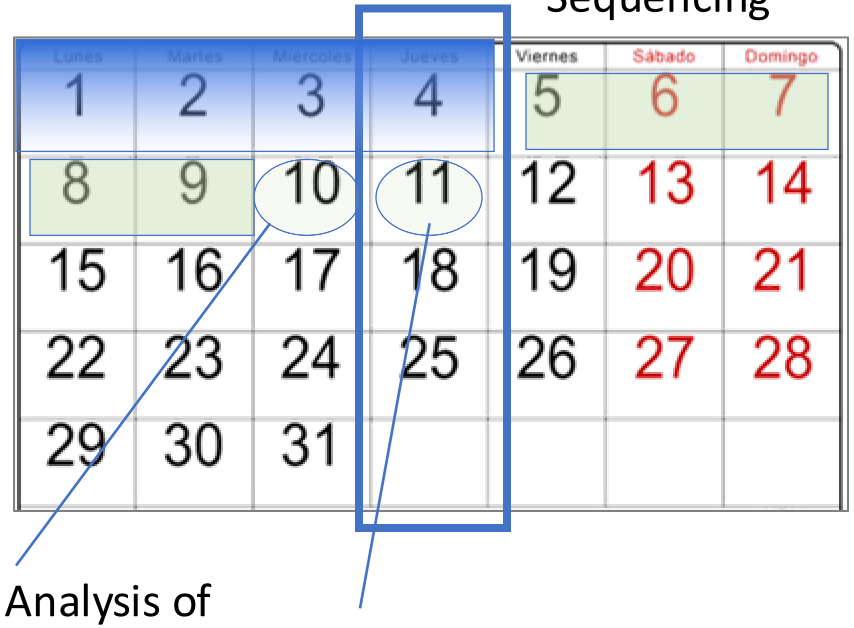


Control of Hospital Transmission

- Microbiology and Infectious Diseases
- Preventive Health
- Laboral Risks
- Genomic Research
- Direction

Outbreaks identification
Nosocomial cases
HCWs infected

Sequencing



Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Sequencing

Analysis of Results

All-parts discussion

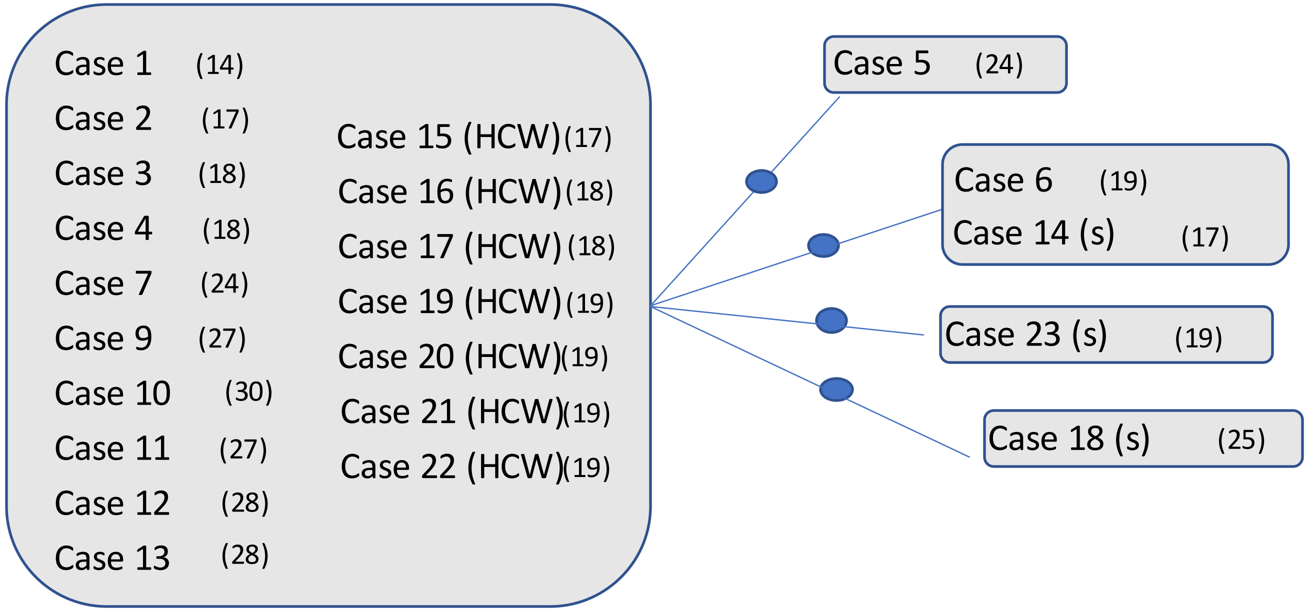
Genomic confirmation of suspected outbreaks

RULE-IN Cases

RULE-OUT Cases

0 SNPs

10 patients
7 HCWs



Case 1 (14)
Case 2 (17)
Case 3 (18)
Case 4 (18)
Case 7 (24)
Case 9 (27)
Case 10 (30)
Case 11 (27)
Case 12 (28)
Case 13 (28)

Case 15 (HCW) (17)
Case 16 (HCW) (18)
Case 17 (HCW) (18)
Case 19 (HCW) (19)
Case 20 (HCW) (19)
Case 21 (HCW) (19)
Case 22 (HCW) (19)

Case 5 (24)

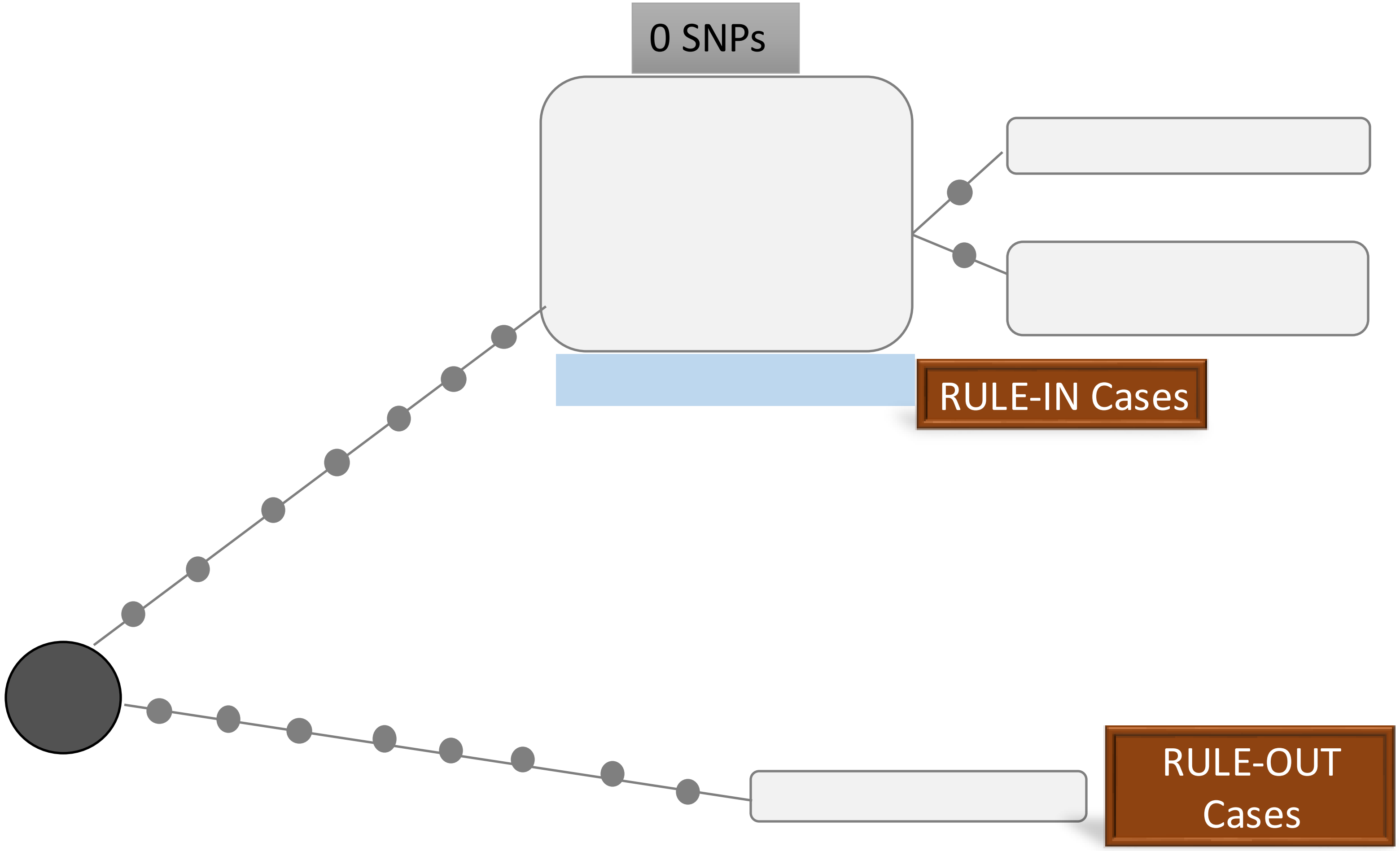
Case 6 (19)
Case 14 (s) (17)

Case 23 (s) (19)

Case 18 (s) (25)

Major nosocomial outbreaks

Monitoring outbreaks after implementing control measures

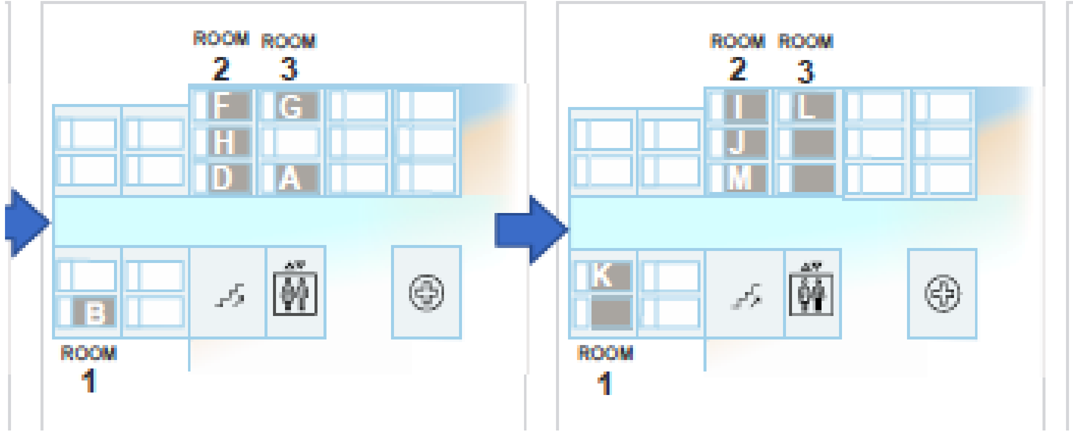


Chracterization of complex outbreaks

Suspected outbreak

Department A

12 patients
1 HCW



Cases from 09/21/2020 to 09/27/2020

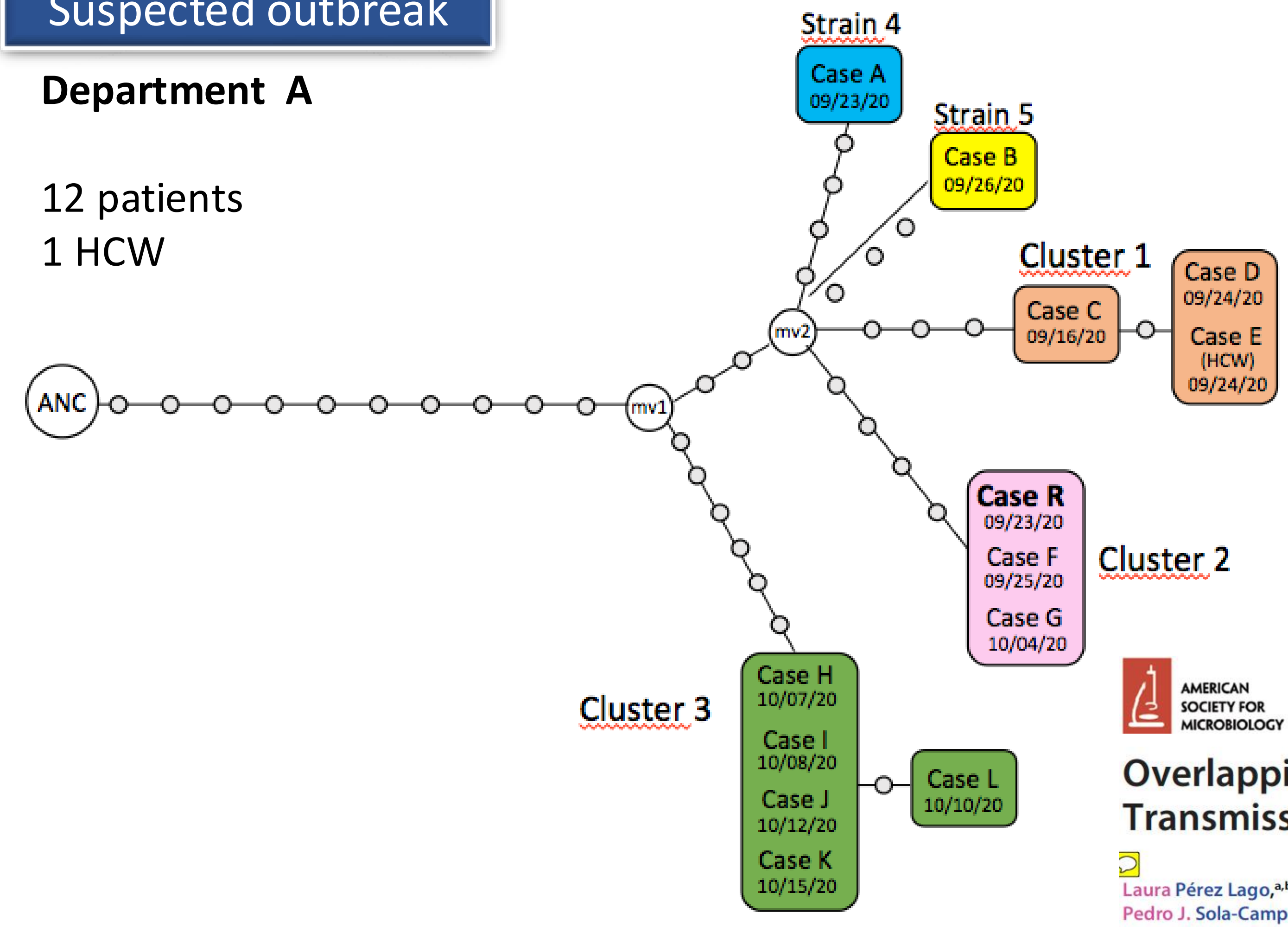
Cases from 10/05/2020 to 10/11/2020

Chracterization of complex outbreaks

Suspected outbreak

Department A

12 patients
1 HCW



Independent introductions

Overlapping outbreaks


AMERICAN SOCIETY FOR MICROBIOLOGY mSphere®

Overlapping of Independent SARS-CoV-2 Nosocomial Transmissions in a Complex Outbreak

Laura Pérez Lago,[a,b] Helena Martínez Lozano,[b,c] Jose Antonio Pajares Díaz,[b,c] Arantxa Díaz Gómez,[b,c] Marina Machado,[a,b] Pedro J. Sola-Campoy,[a,b] Marta Herranz,[a,b,d] Maricela Valerio,[a,b] María Olmedo,[a,b] Julia Suárez González,[b,g] Víctor Quesada Cubo,[b] Maria del Mar Gómez Ruiz,[b,f] Nieves López Fresneña,[b,e] Ignacio Sánchez Arcilla,[b,f] Iñaki Comas,[h,j] Fernando González Candelas,[i] Sonia García de San José,[k] Rafael Bañares,[b,c,l,m] Pilar Catalán,[a,b,d] Patricia Muñoz,[a,b,d,l] Darío García de Viedma,[a,b,d] on behalf of Gregorio Marañón Microbiology-ID COVID-19 Study Group

Chracterization of complex outbreaks

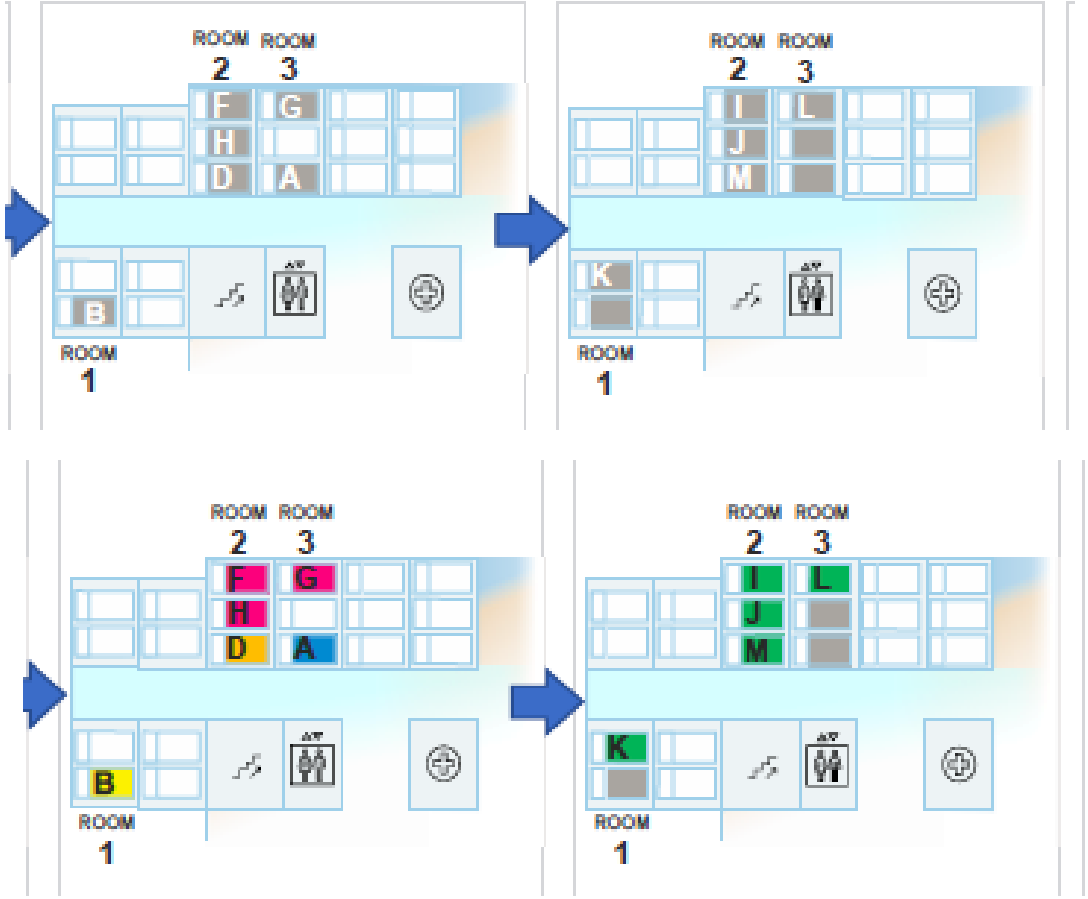
Suspected outbreak

Department A

12 patients
1 HCW

Cases from
09/21/2020 to 09/27/2020

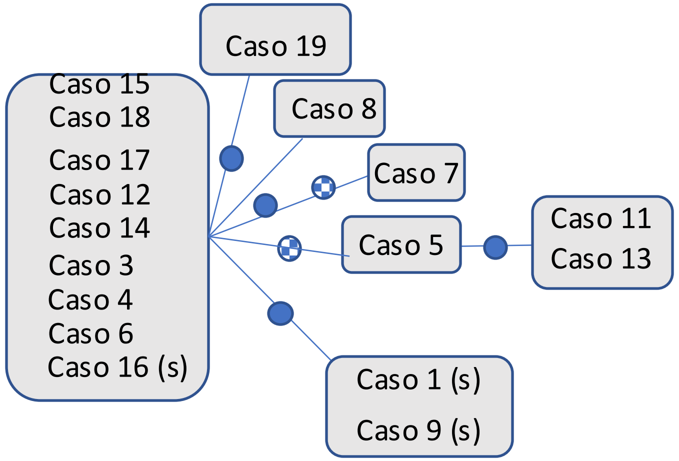
Cases from
10/05/2020 to 10/11/2020



Chracterization of complex outbreaks

Department 1

Firstly: Genomic analysis guided by an outbreak alert



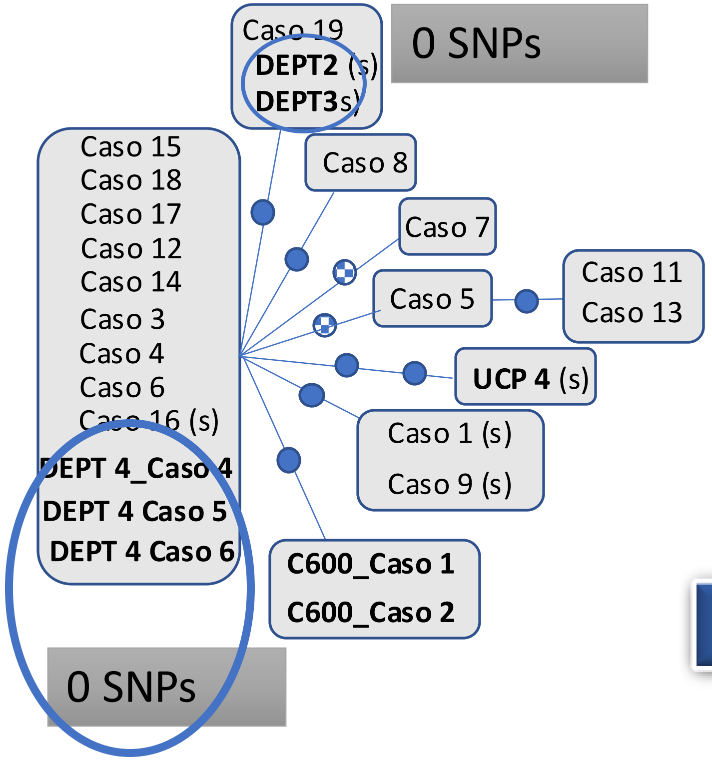
Compare all sequences from different departments among them, without previous assumptions or suspicions

Characterization of complex outbreaks

Department 1

Firstly: Genomic analysis guided by an outbreak alert

Compare all sequences from different departments among them, without previous assumptions or suspicions



Multidepartment transversal outbreak

Transversal links

Outbreak Department 1

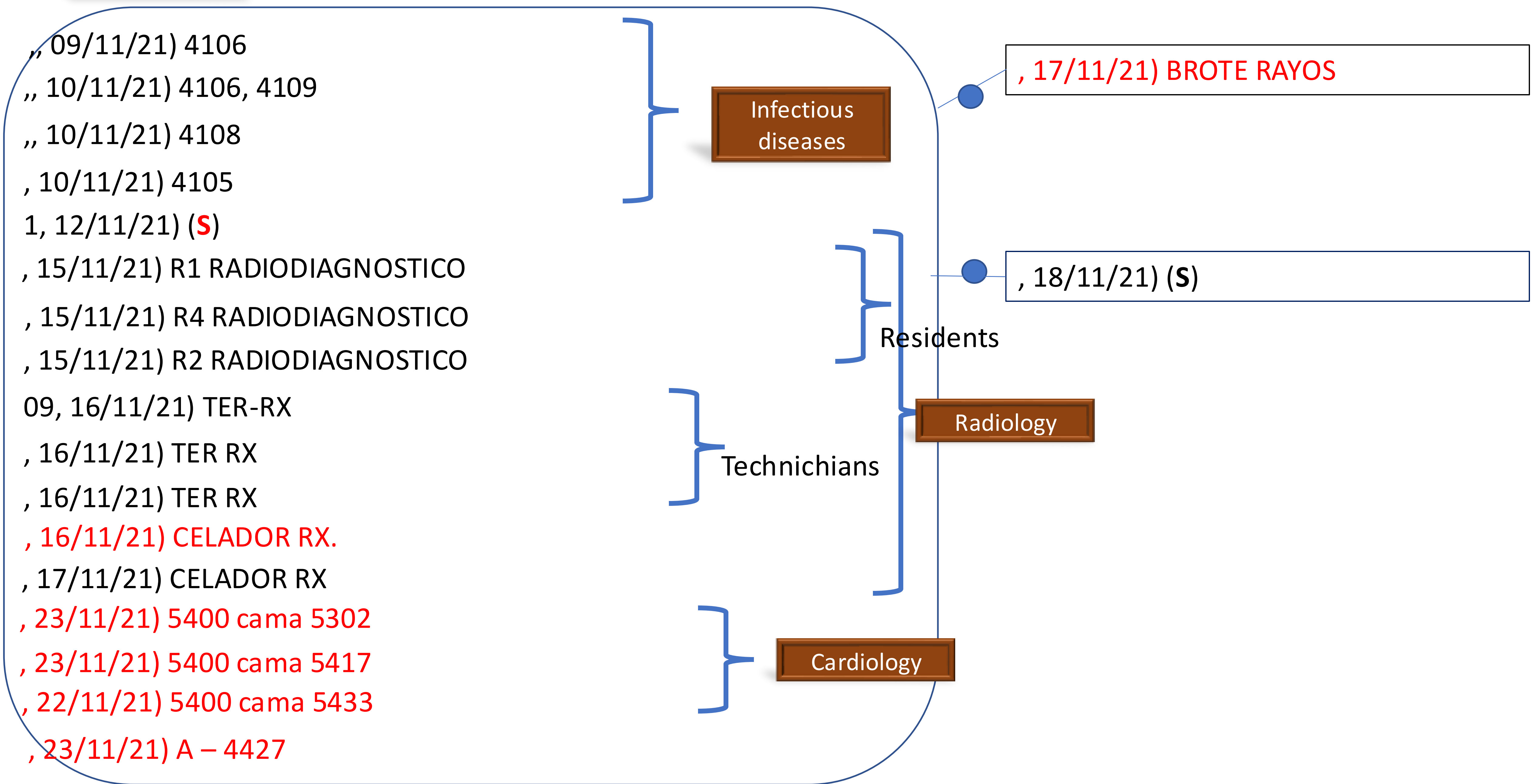
Cases Department 2

Cases Department 3

Cases department 4

Multidepartment transversal outbreaks

0 SNPs



,, 09/11/21) 4106

,, 10/11/21) 4106, 4109

,, 10/11/21) 4108

, 10/11/21) 4105

1, 12/11/21) (**S**)

, 15/11/21) R1 RADIODIAGNOSTICO

, 15/11/21) R4 RADIODIAGNOSTICO

, 15/11/21) R2 RADIODIAGNOSTICO

09, 16/11/21) TER-RX

, 16/11/21) TER RX

, 16/11/21) TER RX

, 16/11/21) CELADOR RX.

, 17/11/21) CELADOR RX

, 23/11/21) 5400 cama 5302

, 23/11/21) 5400 cama 5417

, 22/11/21) 5400 cama 5433

, 23/11/21) A – 4427

Infectious diseases

Residents

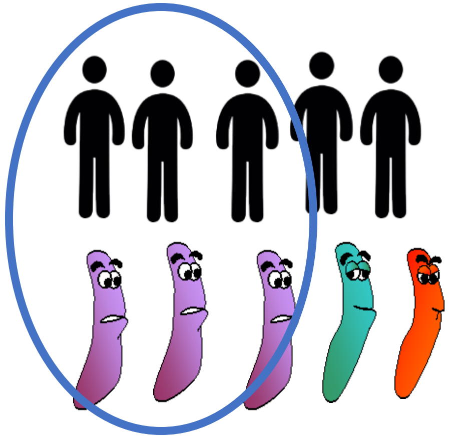
Technichians

Radiology

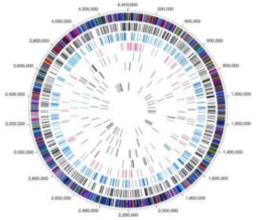
Cardiology

, 17/11/21) BROTE RAYOS

, 18/11/21) (**S**)



Genomic epidemiology

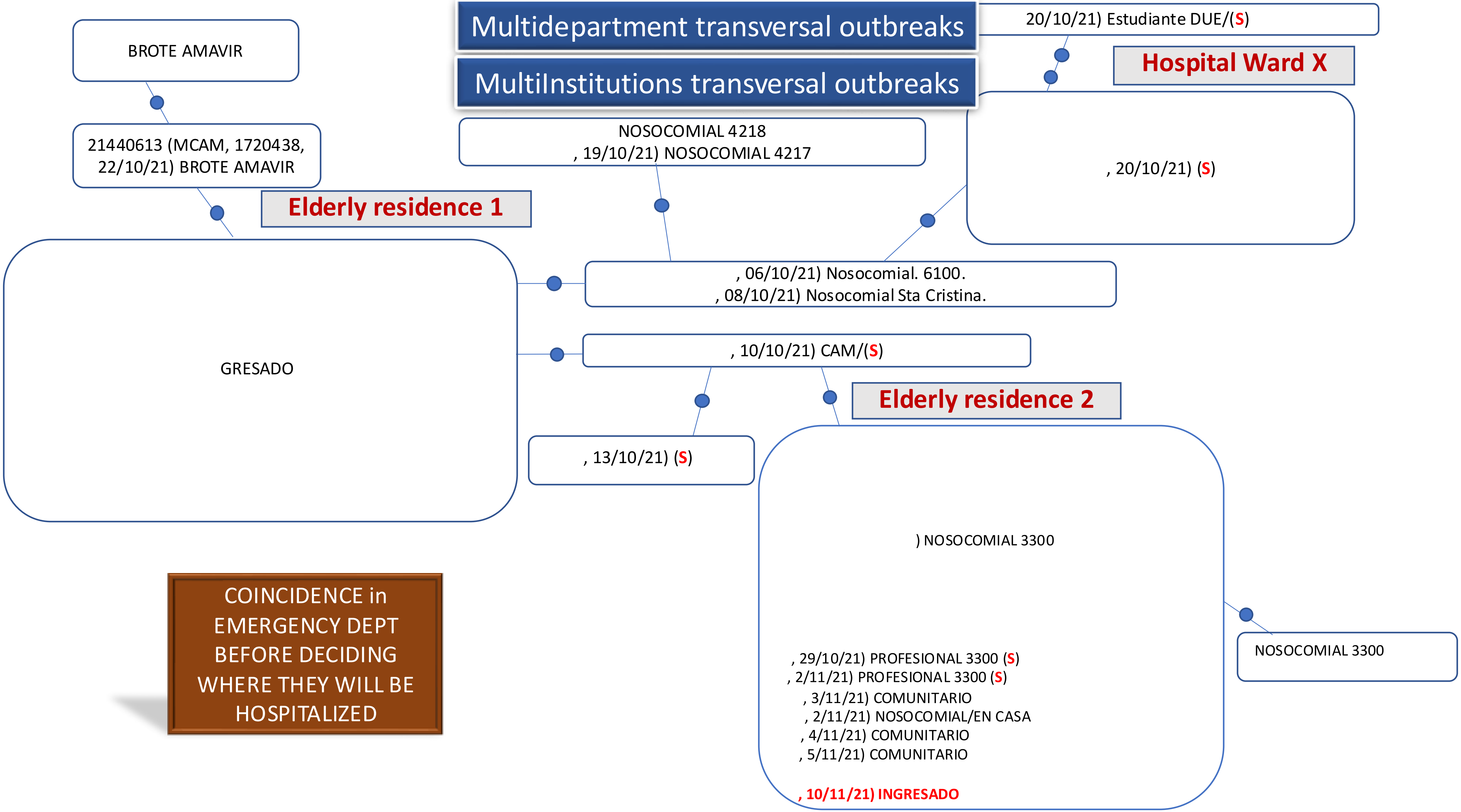


+

Epidemiological data

Multidepartment transversal outbreaks

MultiInstitutions transversal outbreaks



BROTE AMAVIR

21440613 (MCAM, 1720438, 22/10/21) BROTE AMAVIR

Elderly residence 1

GRESADO

NOSOCOMIAL 4218
, 19/10/21) NOSOCOMIAL 4217

20/10/21) Estudiante DUE/(**S**)

Hospital Ward X

, 20/10/21) (**S**)

, 06/10/21) Nosocomial. 6100.
, 08/10/21) Nosocomial Sta Cristina.

, 10/10/21) CAM/(**S**)

, 13/10/21) (**S**)

Elderly residence 2

) NOSOCOMIAL 3300

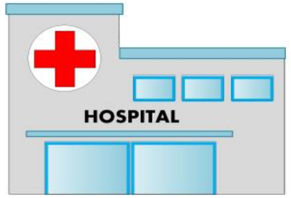
, 29/10/21) PROFESIONAL 3300 (**S**)
, 2/11/21) PROFESIONAL 3300 (**S**)
, 3/11/21) COMUNITARIO
, 2/11/21) NOSOCOMIAL/EN CASA
, 4/11/21) COMUNITARIO
, 5/11/21) COMUNITARIO

, 10/11/21) INGRESADO

NOSOCOMIAL 3300

COINCIDENCE in EMERGENCY DEPT BEFORE DECIDING WHERE THEY WILL BE HOSPITALIZED

Hospital



Control of Nosocomial Transmission

- Microbiology and Infectious Diseases
- Preventive Health
- Laboral Risks
- Genomic Research
- Direction

Precise knowledge of nosocomial dynamics

Tailored interventions

Visitors control

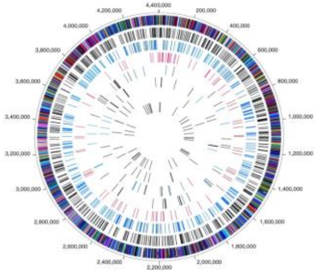
HCWs active screening

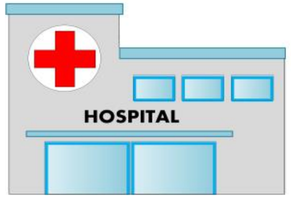
Reduction of intra-hospital mobility

New Multidisciplinary working dynamic sharing a new genomic language

Genomic surveillance Circuit at a Hospital

(Not a research Centre)
And within the pandemic





Response Time

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

72 h

Prolonged quarrantaine

Emphasized Contact tracing

Illumina sequencing

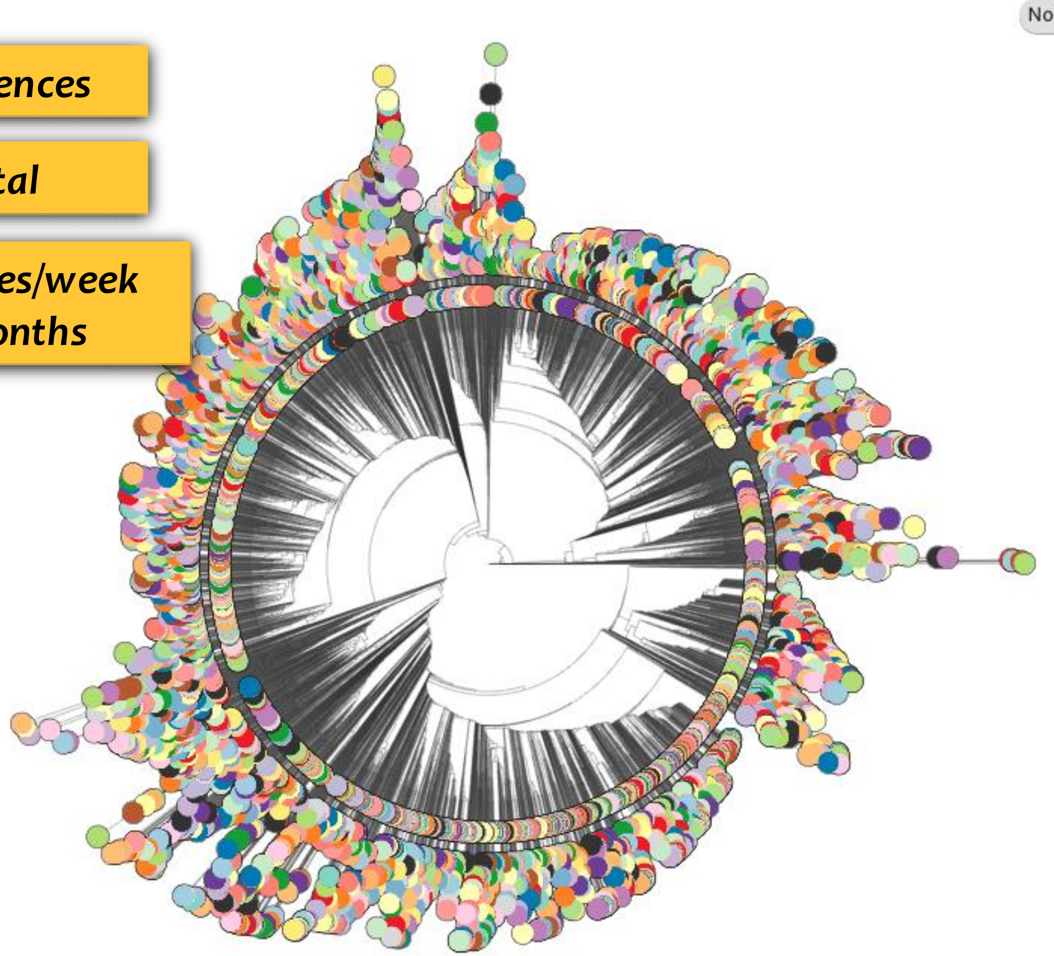
96-120 sequences/week

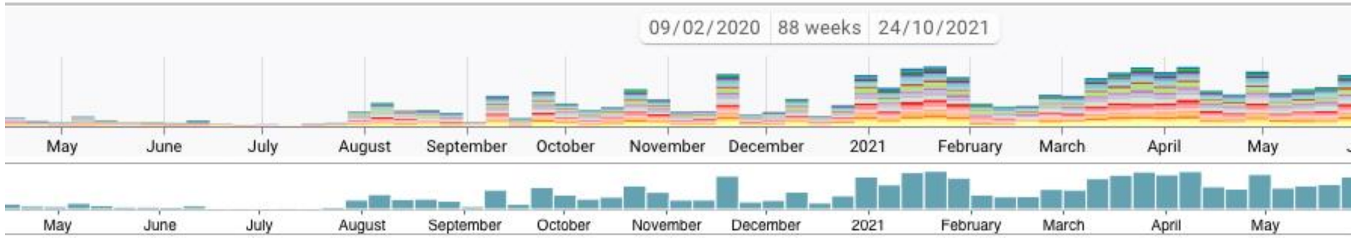
MiSeq/NextSeq

6074 sequences

15% total

75-100% cases/week last 5 months

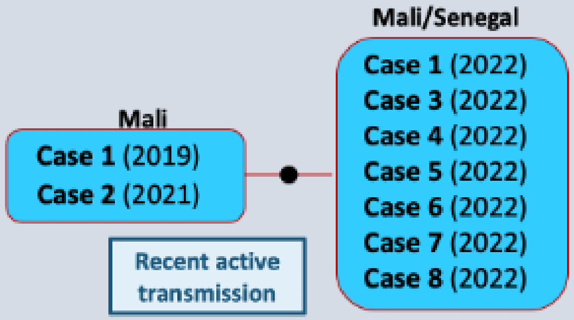


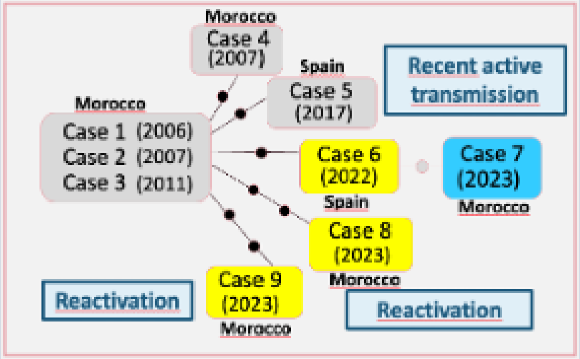


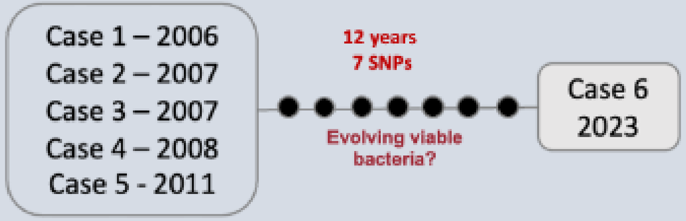
Valuable information: Faster analysis

Evolutionary analysis

Analysis of the **distribution** of SNPs

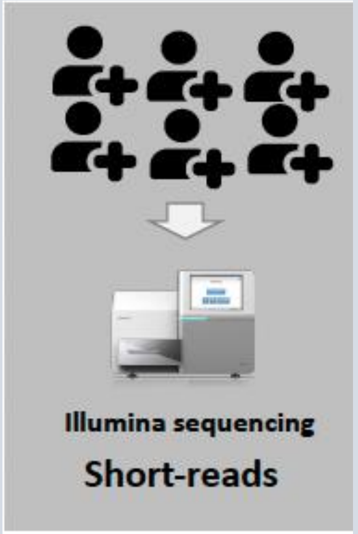






Diagnostic delay +/- Subclinical TB

Illumina sequencing

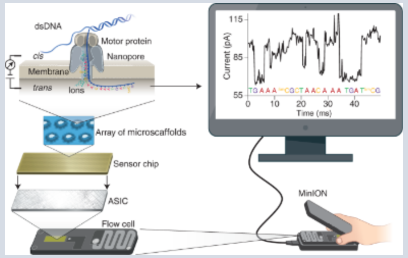


-Pooled in the same run

-Subcultured isolates

Delayed results

Nanopore sequencing

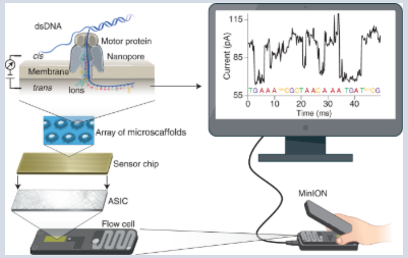


Real-time analysis

Speed
Flexibility

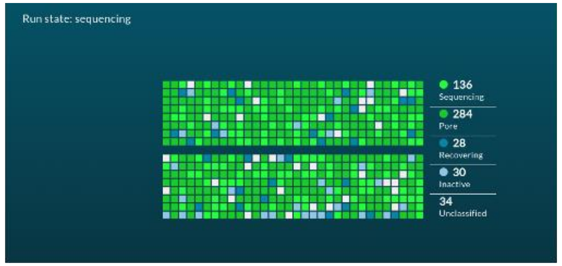
Genomic surveillance Circuit from a Hospital

Nanopore sequencing



Real-time analysis

Speed
Flexibility



Minion Sequencing

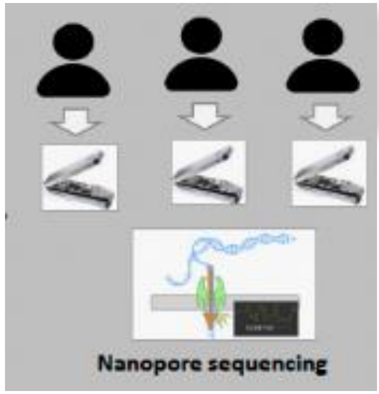
1-16 sequences/run

Illumina sequencing

-Pooled in the same run

-Subcultured isolates

Nanopore sequencing



One incident case, inmediate analysis

Speed
Flexibility

March-July 2023

Isolate	Flow-cell usages	Mean coverage	% Genome coverage >20X	Run time	
1	A	80,88	96,49	1h 13min	Orphan
2	B	48,51	94,6	24h 48min	Clustered
3	C	91	95,91	1h 50min	Orphan
4		50,33	93,02	1h 50min	Orphan
5	C	48,47	94,05	4h 4 min	Orphan
6	C	36,02	92,18	2h 37 min	Orphan
7	C	76,68	96,63	1h 13 min	Orphan
8	C	72,73	95,64	[illegible]	Clustered
9	C	81,94	96,29	[illegible]	Orphan
10		54,91	95,01	4h 00min	Orphan
11	D	70,91	95,59	51 min	Orphan
12	D	86,82	96,53	1h 23 min	Clustered
13		59,68	95,42	2h 49 min	Orphan
14	D	72,36	95,84	1h 35 min	Clustered
15	E	76,84	94,69	1h 11min	Clustered
16	F	74,74	96,49	2h 28 min	Orphan
17	E	75,32	95,99	3h 11min	Clustered
18	F	87,58	96,46	3h 58min	Orphan
19	E	78,72	97,27	1h 24 min	Clustered
20	F	72,59	96,76	1h 29 min	Clustered
21	E	73,42	97,34	3h 4min	Clustered
22	F	73,65	97,46	2h 24min	Orphan
23	G	68,24	96,1	2h 18min	Orphan

50%
< 2 hours

Genomic epidemiology

1. *Mycobacterium tuberculosis*

2. SARS-CoV-2

3. Nosocomial transmission

Vulnerable patients
MDR bacteria

Klebsiella michiganensis VIM Padiatric Oncology

Pseudomonas aeruginosa XDR ICU

Serratia UCCQ

Pseudomonas UCCQ

Serratia UCI Neonatology

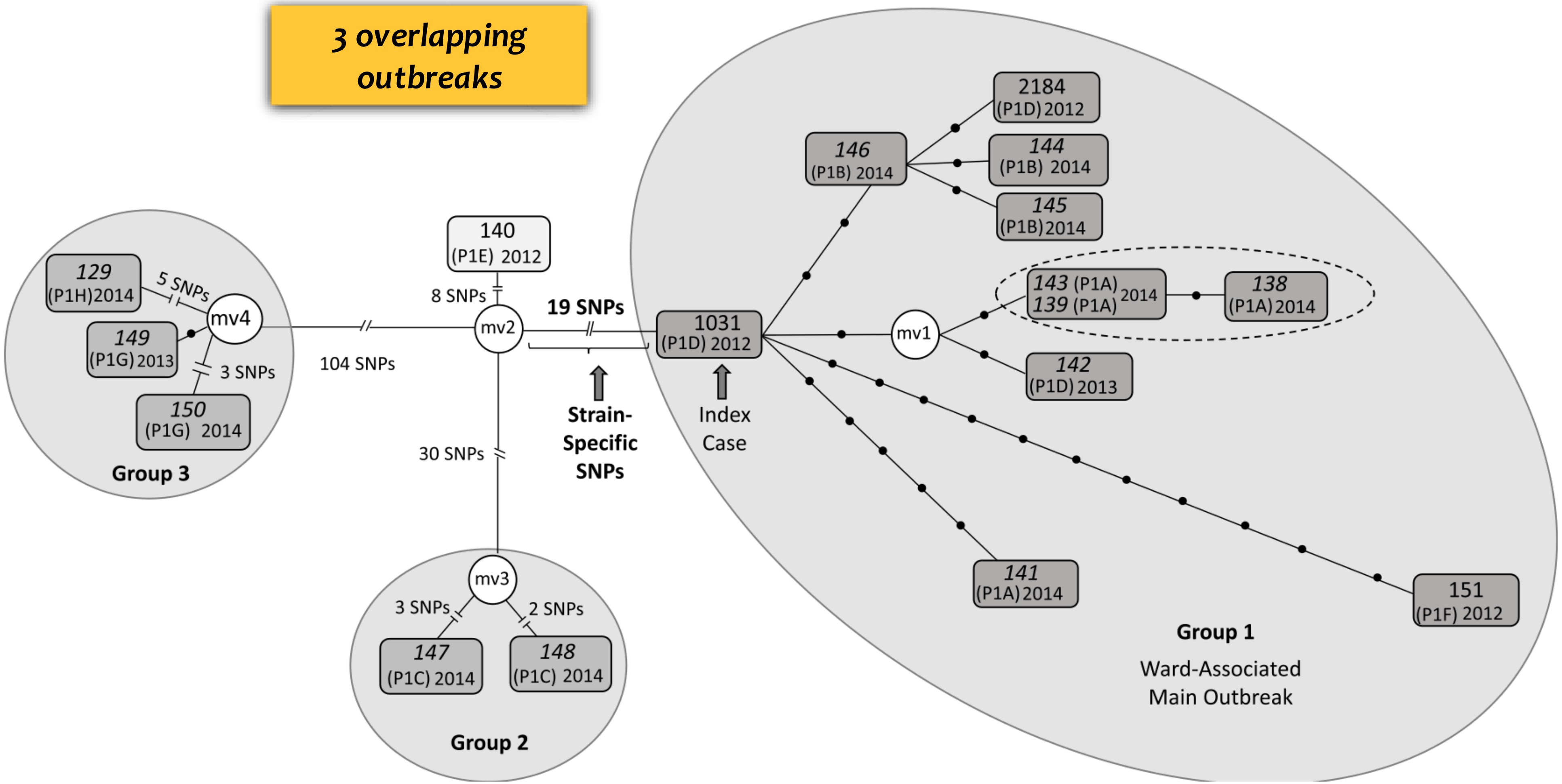
MDR *Pseudomonas aeruginosa*

outbreak alert

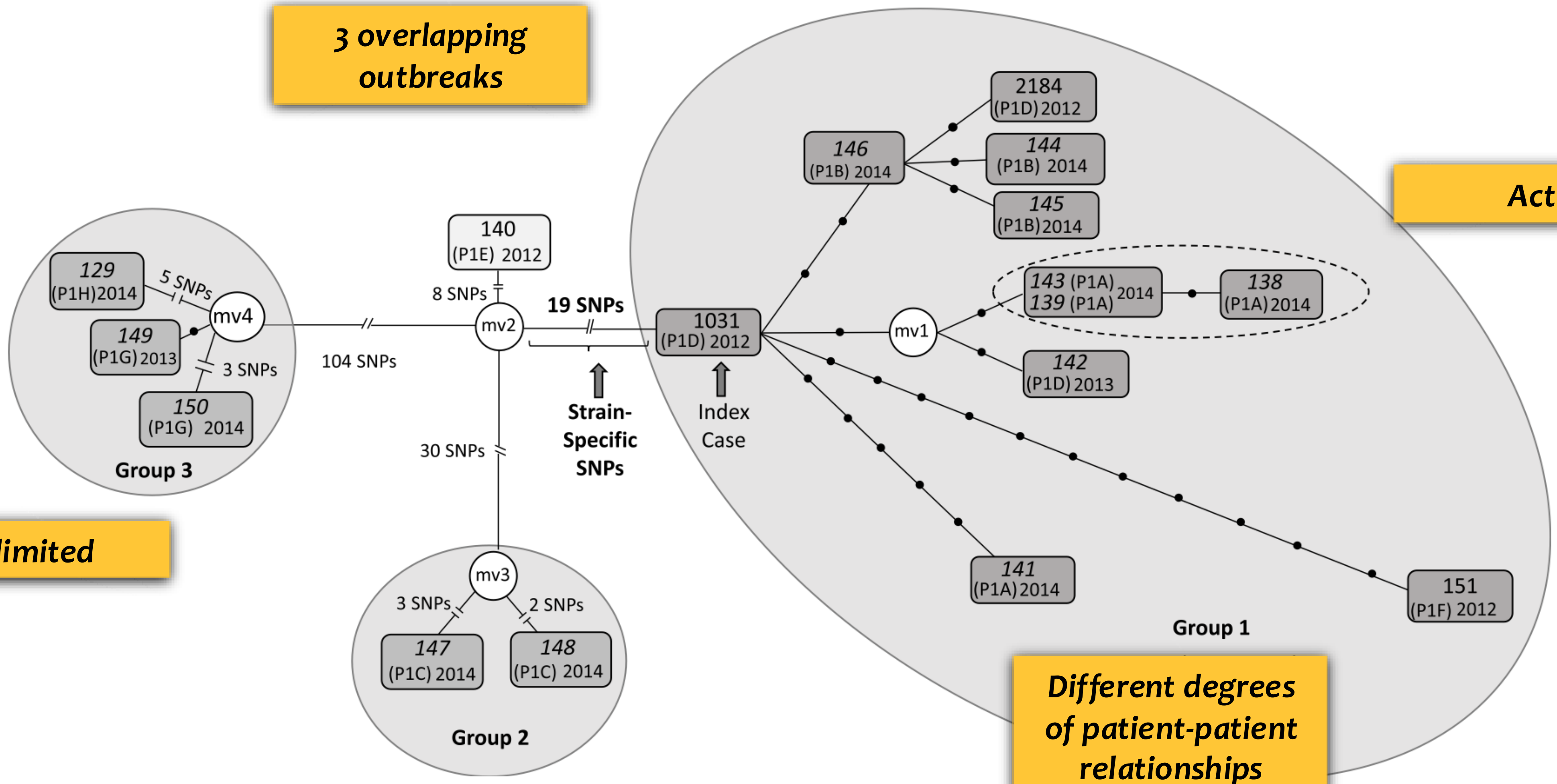
in Haematology ward

MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward

3 overlapping outbreaks



MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward



3 overlapping outbreaks

Active

Self-limited

Self-limited

Different degrees of patient-patient relationships

Serratia marcescens ICU Neonatology

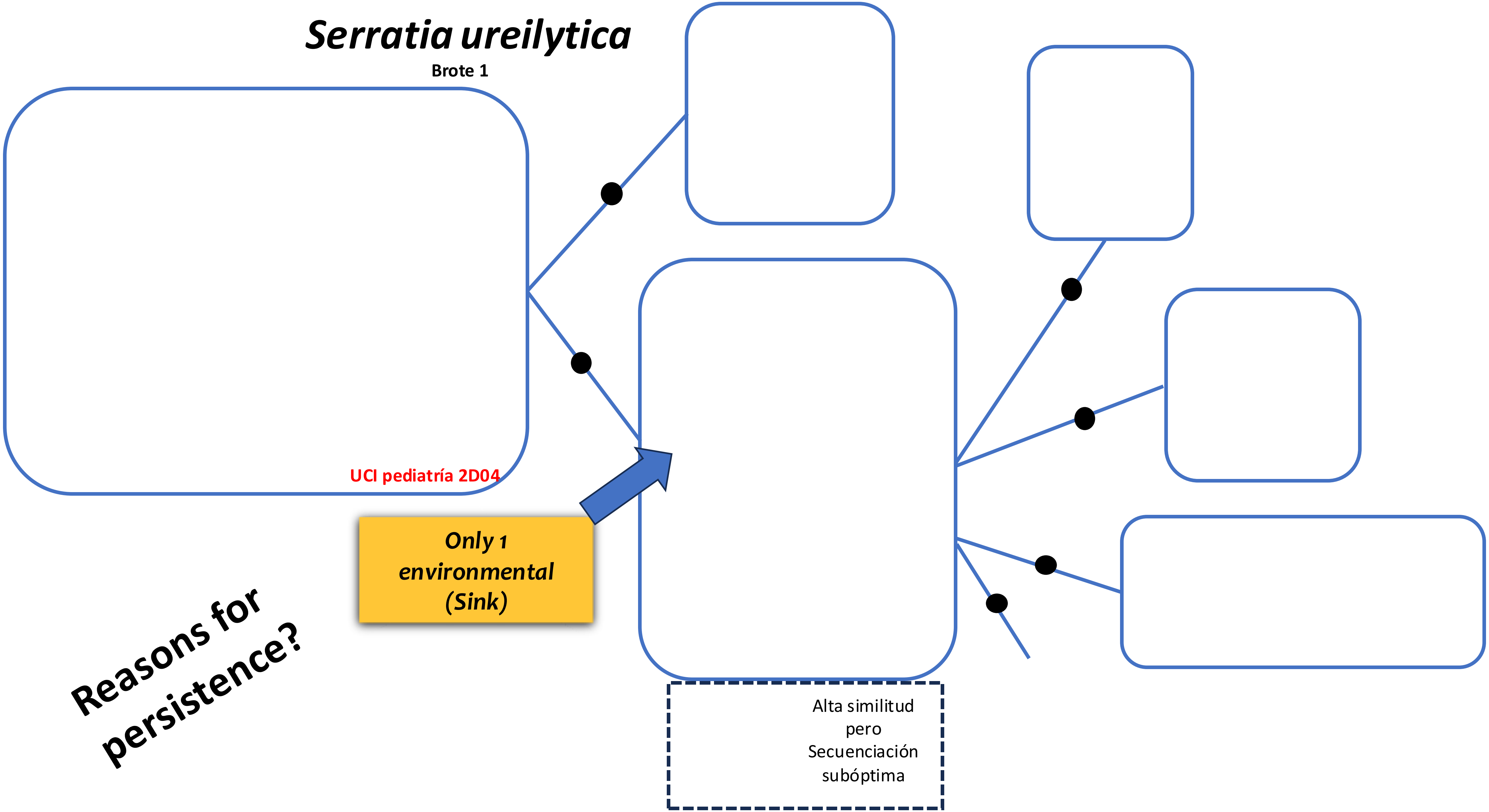
along 5 months

Outbreak 1
Serratia ureilytica

17 cases

Serratia ureilytica

Brote 1



UCI pediatría 2D04

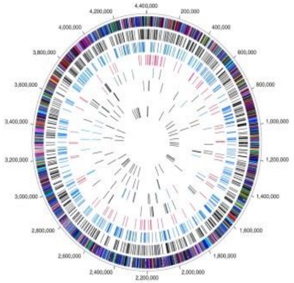
Only 1 environmental (Sink)

Alta similitud
pero
Secuenciación
subóptima

Reasons for persistence?

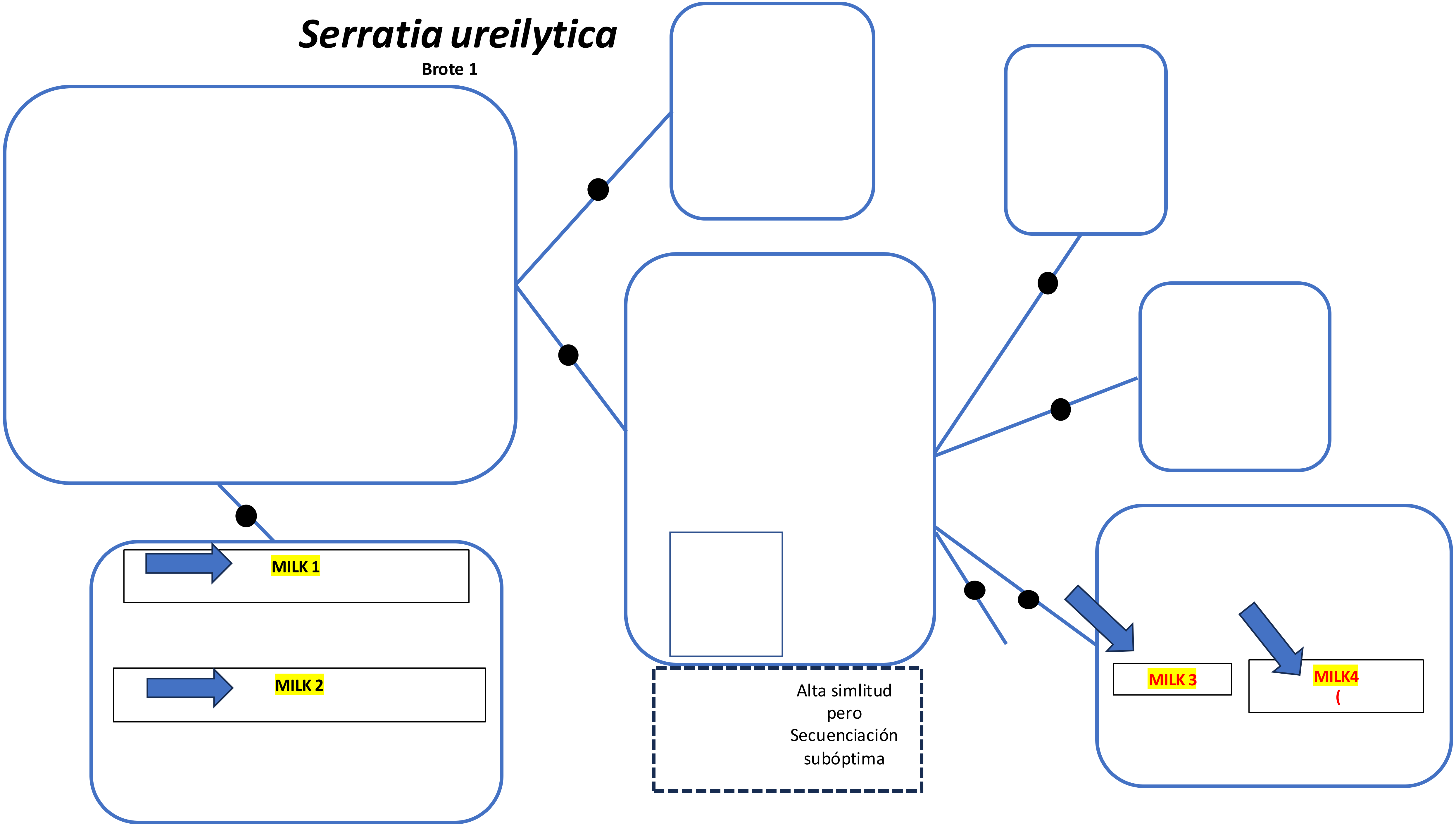
Breast milk donated for other kids (MILK bank): Sterilized but control cultures

Serratia



Serratia ureilytica

Brote 1



MILK 1

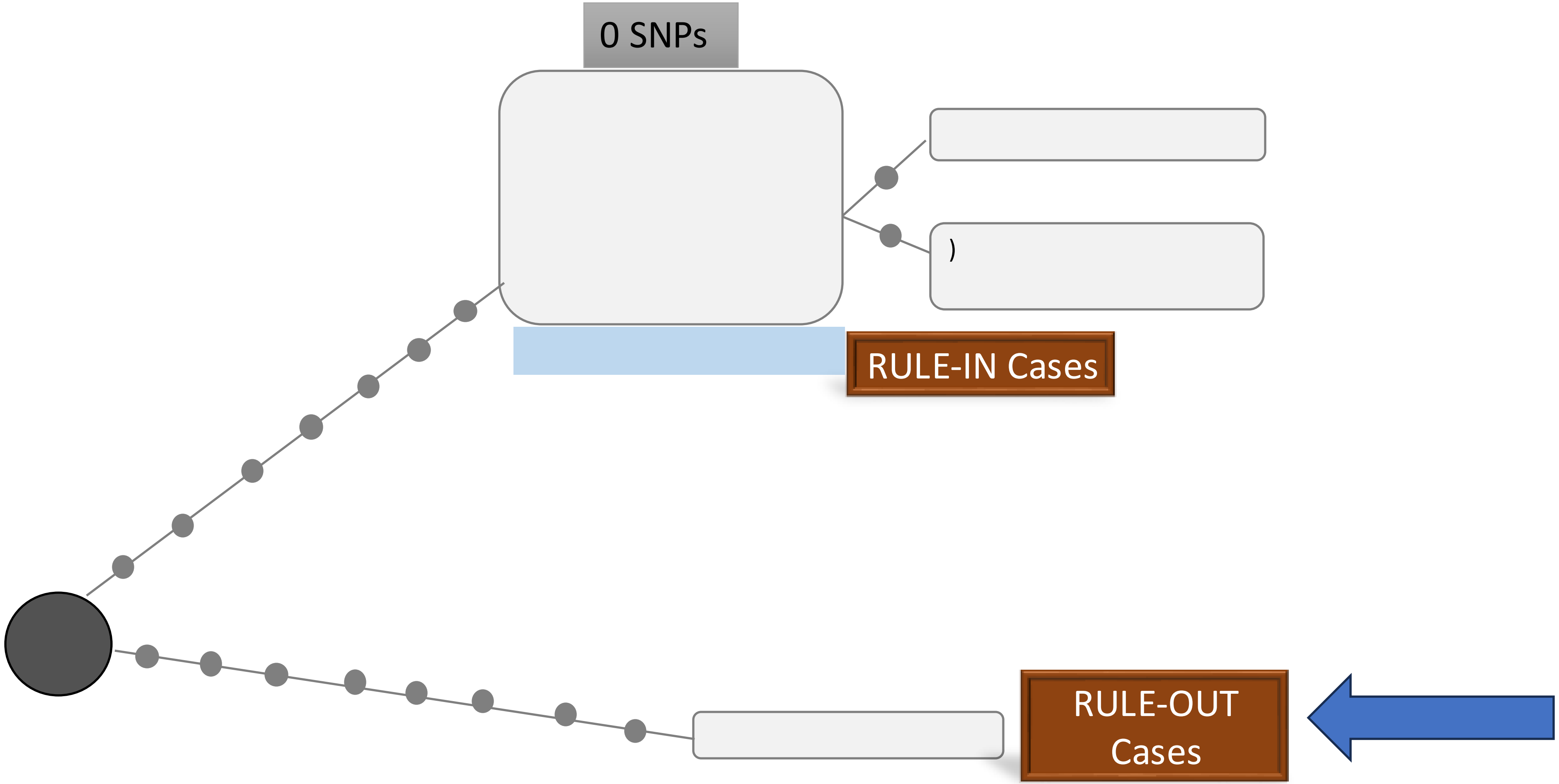
MILK 2

Alta simlitud
pero
Secuenciación
subóptima

MILK 3

MILK4
(

Monitoring outbreaks after implementing control measures




4,400,000
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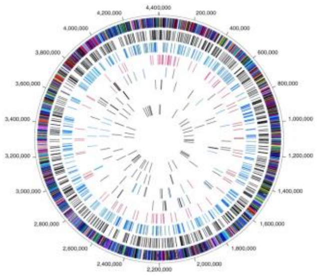
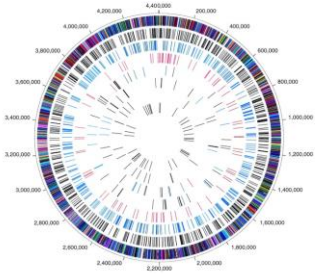
4,200,000


dreamstime.com



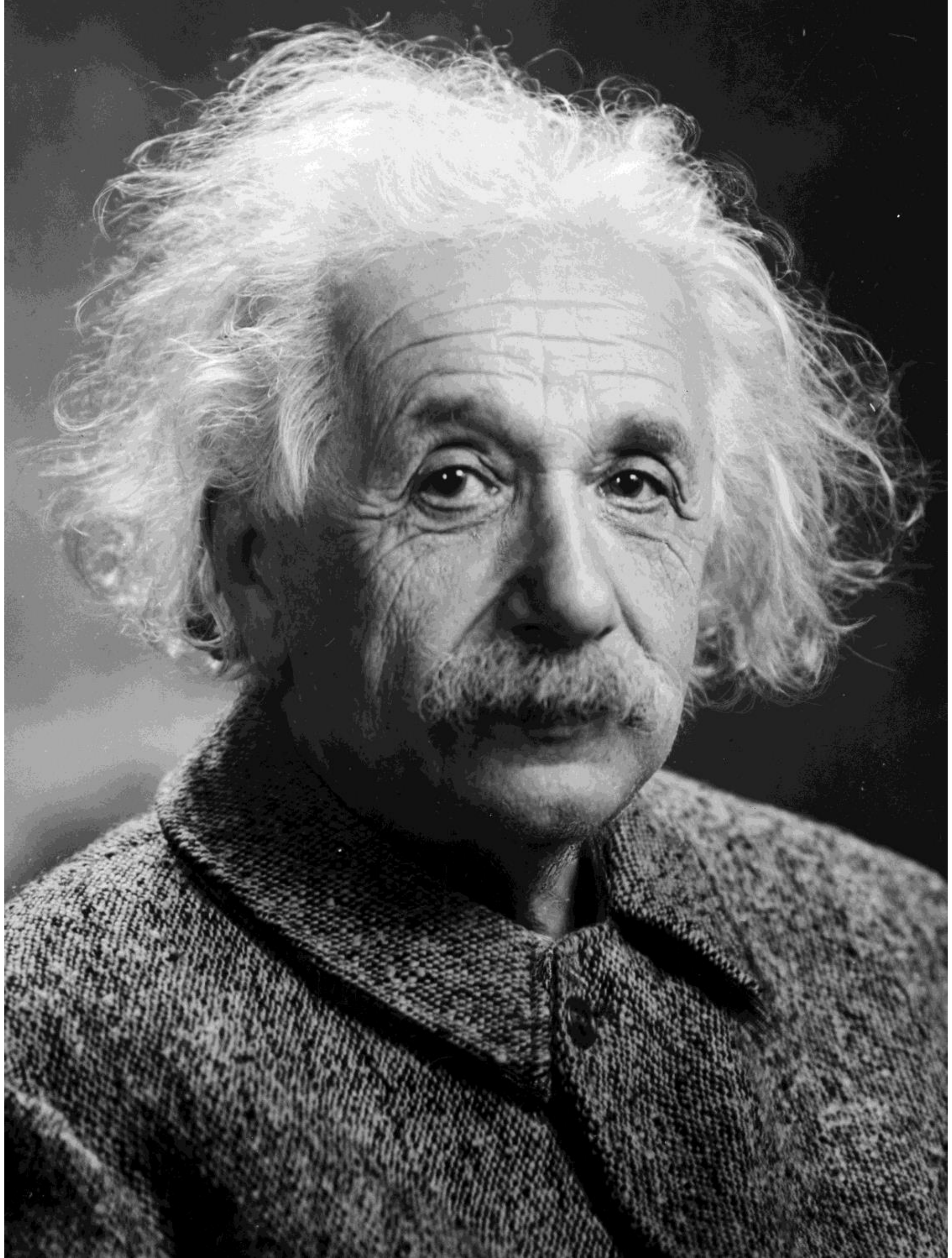
Identify informative simple markers

Target them with simple tools to allow FAST high-confident pre-identification



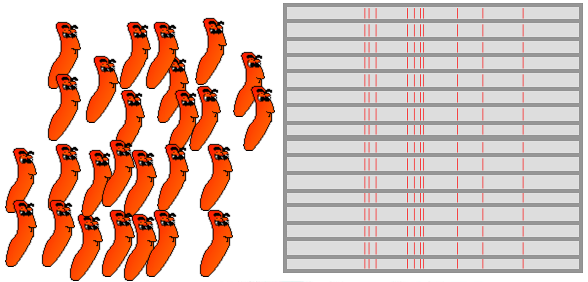
Identify informative simple markers

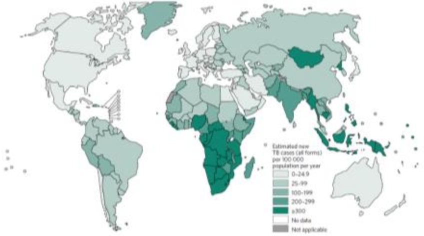
Target them with simpler tests to allow FAST high-confident pre-identification

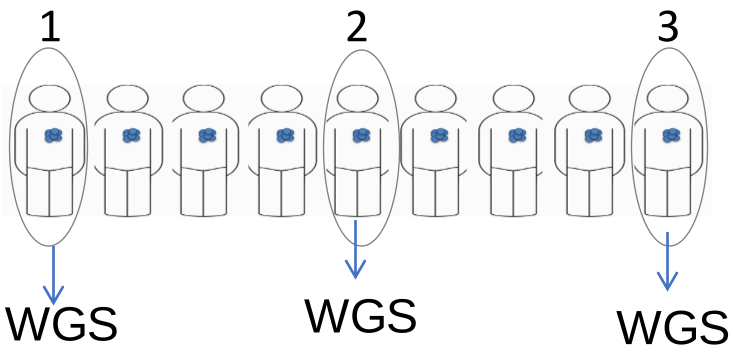


Our proposal

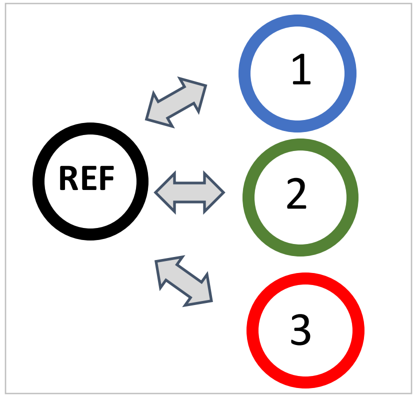
1

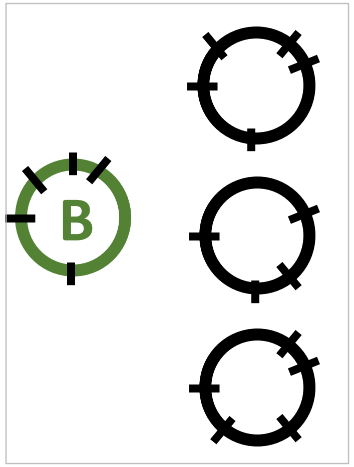


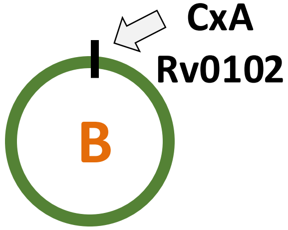




2





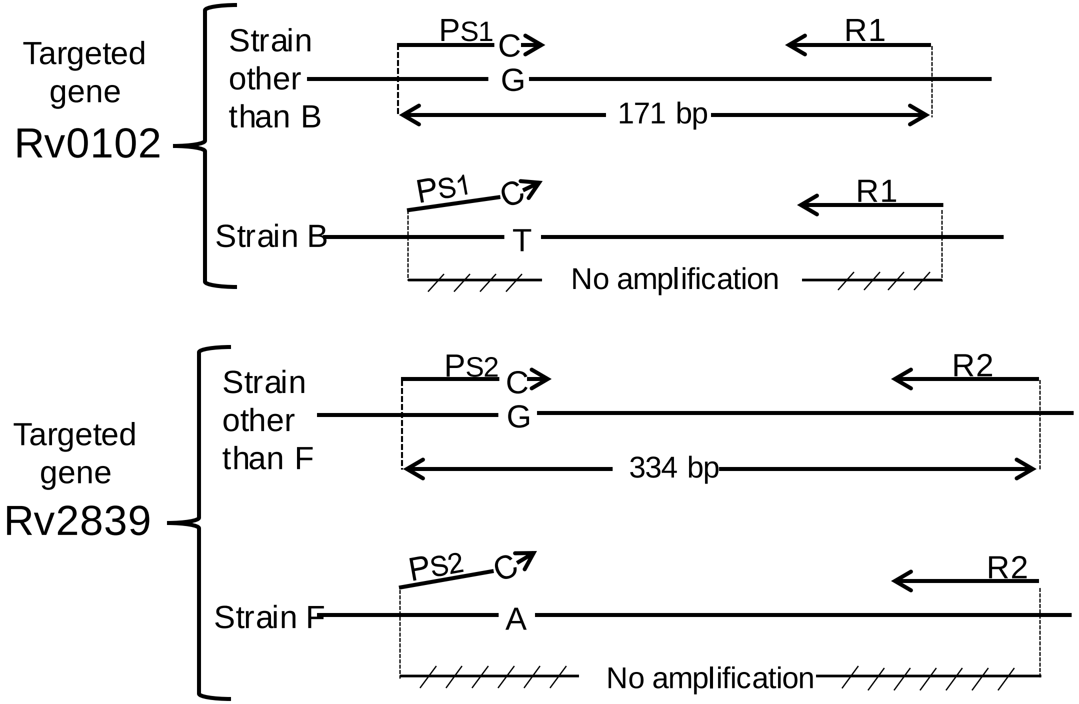


Strain Specific SNPs

User-friendly approach

Targeted Regional Alelle-specific PCR (TRAP)

Strain-specific PCRs



Targeted gene Rv0102

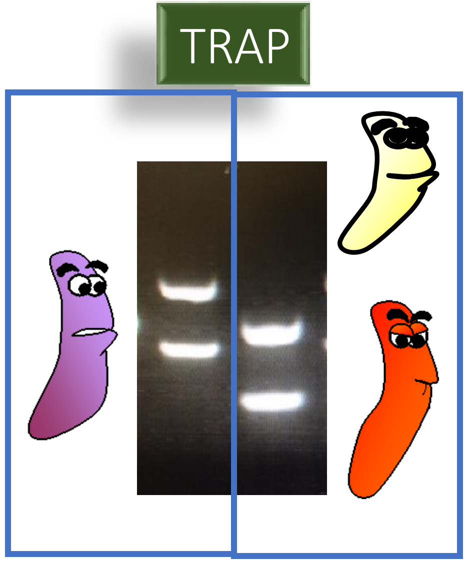
Strain other than B
PS1 C
G
R1
171 bp

Strain B
PS1 C
T
R1
No amplification

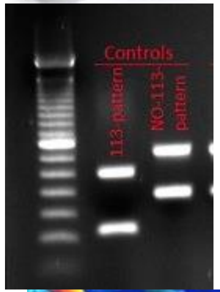
Targeted gene Rv2839

Strain other than F
PS2 C
G
R2
334 bp

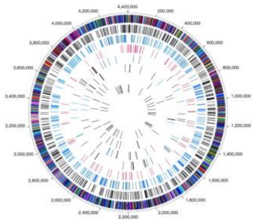
Strain F
PS2 C
A
R2
No amplification



TRAP




designed by freepik.com

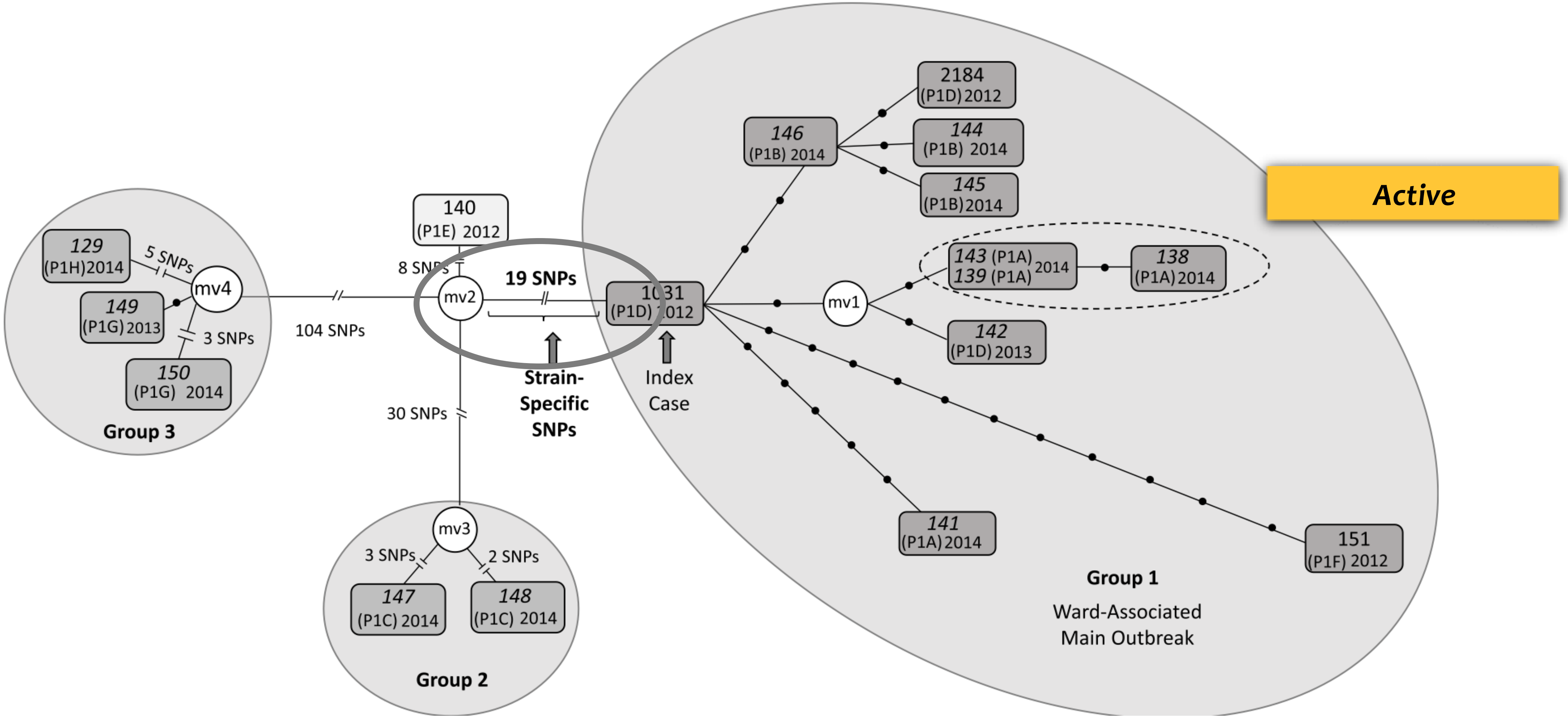


Mycobacterium tuberculosis

Peru
Panama
Costa Rica
Somalia

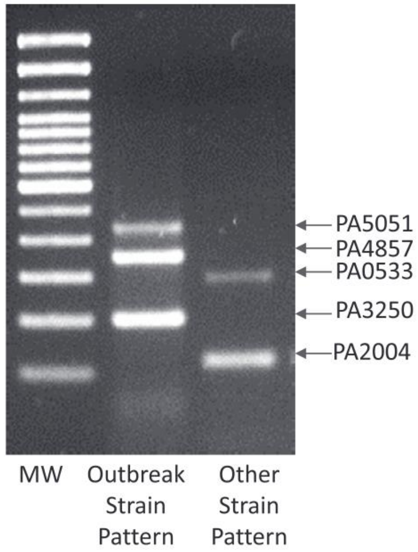
Italy
France
Portugal

MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward

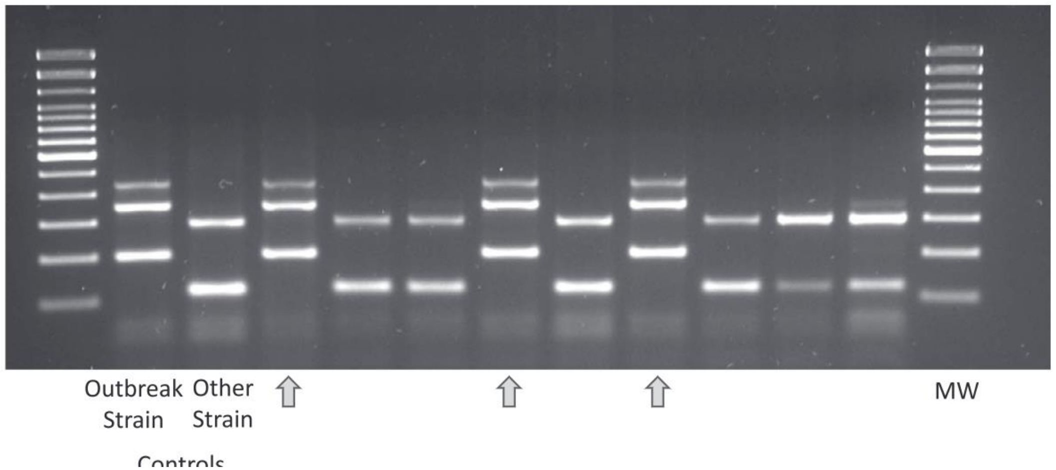


Active

A)

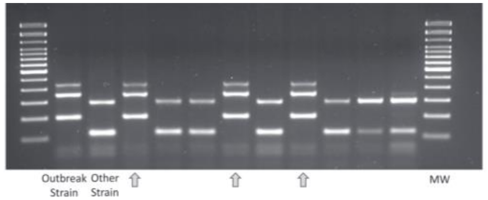

PA5051
PA4857
PA0533
PA3250
PA2004
MW
Outbreak Strain Pattern
Other Strain Pattern

B)

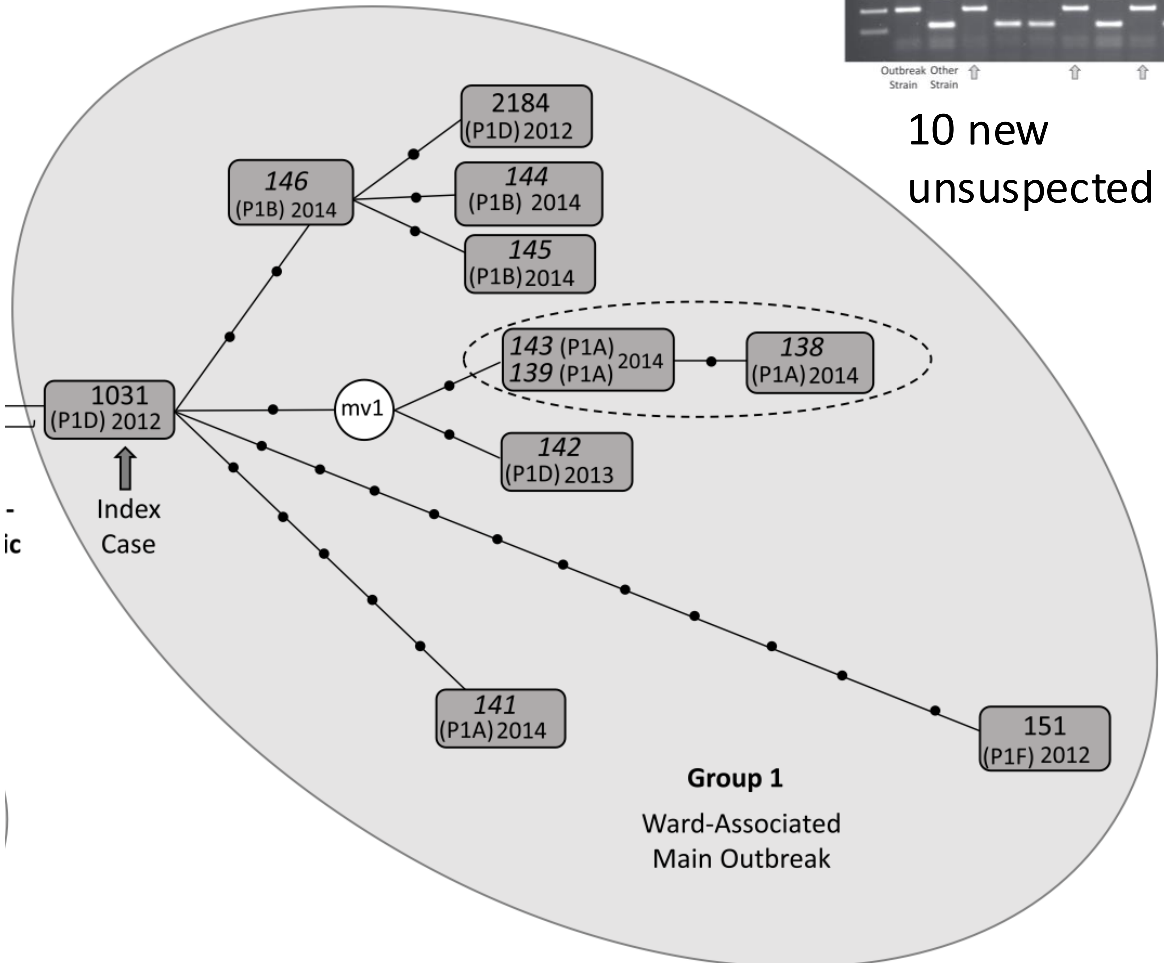

Outbreak Strain
Other Strain
Controls
MW

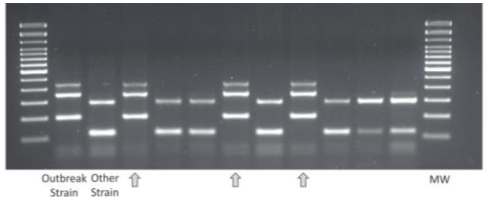

DAIREI
CRYOBANK

Active

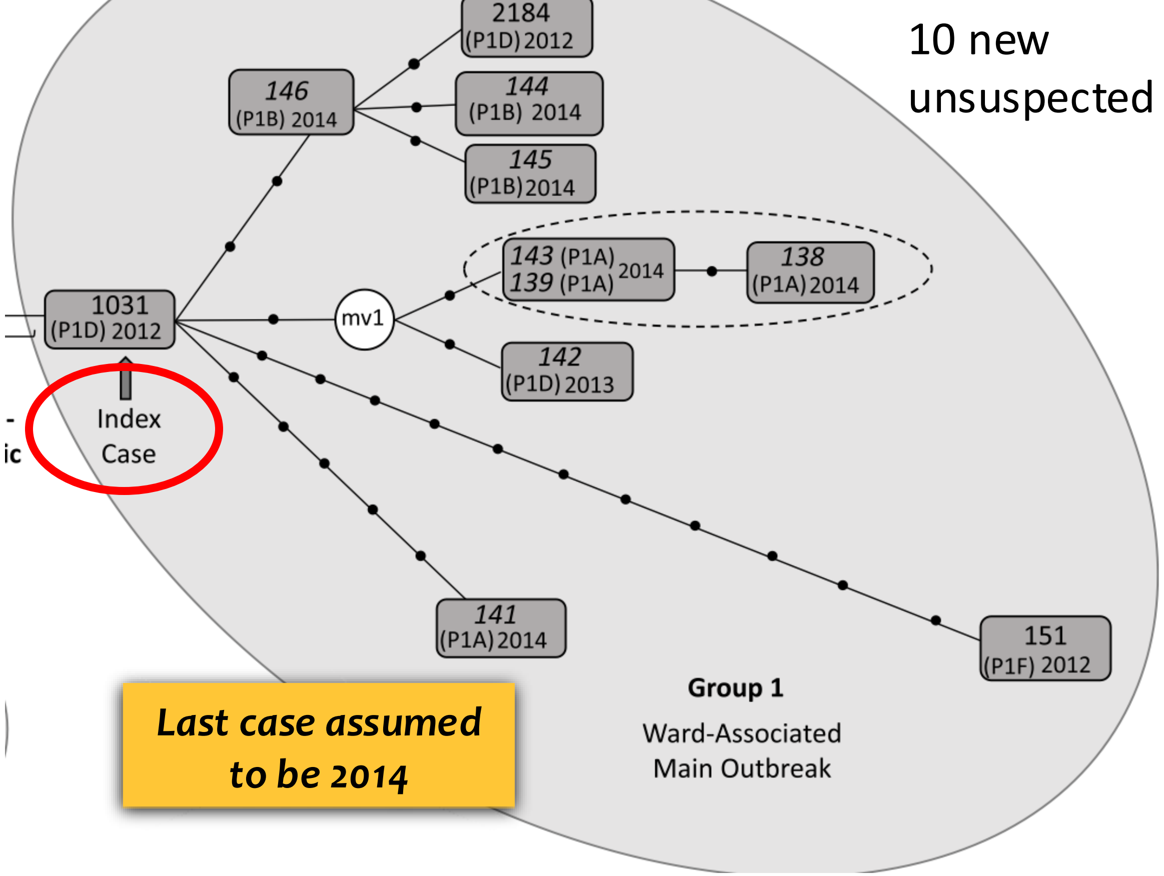


10 new
unsuspected cases



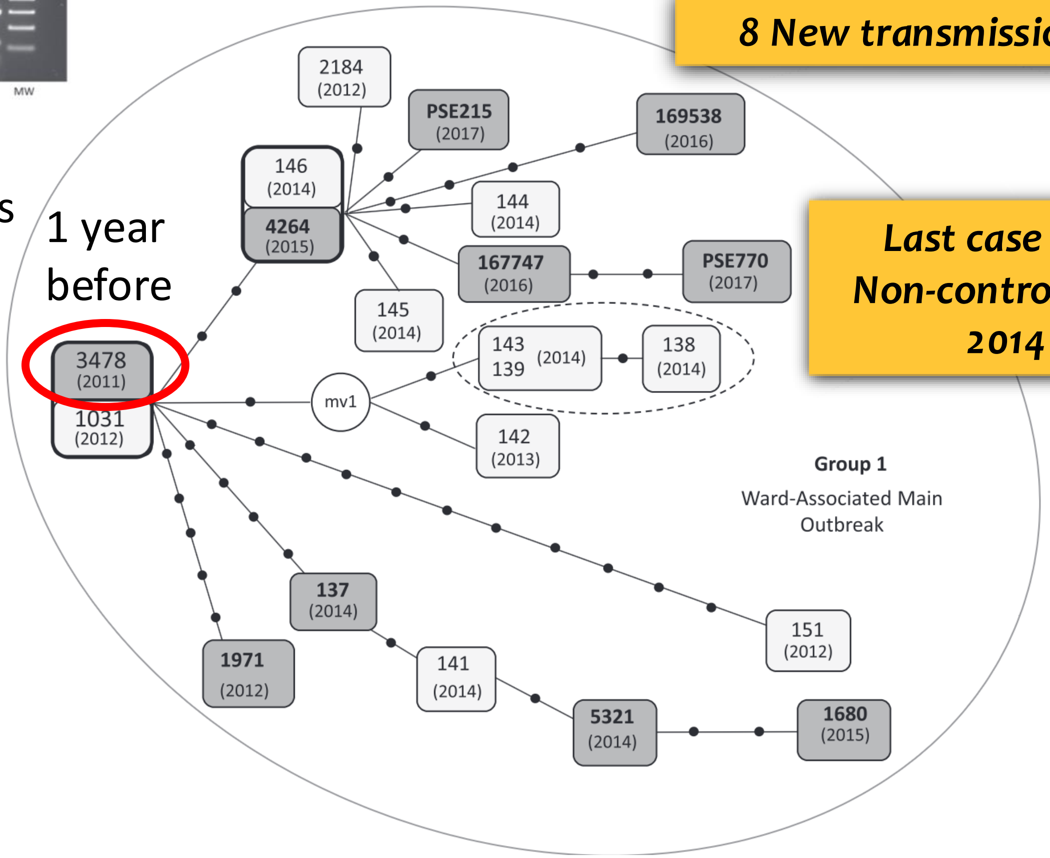


10 new unsuspected cases



Last case assumed to be 2014

1 year before



8 New transmissions

Last case 2017 Non-controlled in 2014